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Ministry of Health & Family Welfare

Pharmacopoeia of India

(The Indian Pharmacopoeia)

ADDENDUM (II)

TO

Third Edition
(1985)

सत्यमेव जयते

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PUBLISHED BY THE CONTROLLER OF PUBLICATIONS, DELHI
1991

Pharmacopoeia of India

(The Indian Pharmacopoeia)

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गुरुकुल कांगड़ी विश्वविद्यालय
विषय संख्या ______ आगत नं० 108833
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ADDENDUM (II)

To

Pharmacopoeia of India
(Indian Pharmacopoeia)
Third Edition

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Pharmacopoeia of India

(The Indian Pharmacopoeia)

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ADDENDUM (II)

TO

Third Edition
(1985)

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Notices

The Addendum II to the Pharmacopoeia of India 1985 amends the Indian Pharmacopoeia 1985 and Addendum I and constitutes a part of Indian Pharmacopoeia, Third Edition.

The General Notices and Appendices included in the Indian Pharmacopoeia 1985 and Addendum I and as amended in this Addendum apply both to the matter contained in the Indian Pharmacopoeia 1985, Addendum I and to the matter contained in this Addendum.

LEGAL NOTICES

In India there are laws dealing with certain of the substances which are the subject of monographs which follow. These monographs should be read subject to the restrictions imposed by those laws wherever they are applicable.

It is expedient that enquiry be made in each case in order to ensure that the provisions of any law are being complied with.

In general, the Drugs and Cosmetics Act, 1940, the Narcotic Drugs and Psychotropic Substances Act, 1985 and the Poisons Act, 1919, and the rules framed thereunder should be consulted.

Under the Drugs & Cosmetics Act, the Indian Pharmacopoeia is the book of standards for drugs included therein and the standards as included in the Indian Pharmacopoeia would be official. If considered necessary these standards can be amended and the Secretary of the Indian Pharmacopoeia Committee is authorised to issue such amendments. Whenever such amendments are issued, the Indian Pharmacopoeia would be deemed to have been amended accordingly.

PATENTS AND TRADEMARKS

The inclusion in the Indian Pharmacopoeia of any drug subject to actual, or potential, patent or similar rights, or the inclusion of any name which is a trademark in any part of the world does not and shall not be deemed to imply or convey permission, authority, or licence to exercise any right or privilege protected by such patent or trademark, including licence to manufacture, without due permission, authority, or licence from the person or persons in whom such rights and privileges are vested.

Preface

This Addendum amends the Indian Pharmacopoeia 1985 and Addendum I and is published by Government of India, Ministry of Health and Family Welfare on the recommendation of Indian Pharmacopoeia Committee (in accordance with Drugs & Cosmetics Act, 1940, the Narcotic Drugs and Psychotropic Substances Act, 1985 and the Poisons Act, 1919, and the rules framed thereunder).

The Government of India constituted a permanent Indian Pharmacopoeia Committee in 1948 for the preparation of the Indian Pharmacopoeia and keeping it up-to-date. The first edition of the Indian Pharmacopoeia was published in 1955, followed by a Supplement in 1960. The second edition of the Indian Pharmacopoeia and its Supplement were published in 1966 and 1975 respectively. The third edition of the Indian Pharmacopoeia was published in 1985.

The Government of India, Ministry of Health & Family Welfare, vide Resolution No. X.19014/2/83-DMS&PFA dated 18th January, 1984 reconstituted the Indian Pharmacopoeia Committee with the following as members for a term of five years for the purpose of compilation of the Supplement to the third edition of the Indian Pharmacopoeia:

Chairman	Dr. Nitya Nand, Ph.D., F.N.A. Ex-Director Central Drug Research Institute Lucknow.
Member	Dr. P.L. Sharma, M.D., Ph.D. (London), F.A.M.S. Prof. of Pharmacology, Post-Graduate Institute of Medical Education and Research, Chandigarh.
Member	Dr. B.M. Hegde, M.D., F.R.C.P. (London), F.R.C.P. (Edin), F.R.C.P. (Glasgow), F.A.C.C. Prof. of Medicine and Principal, Kasturba Medical College, Mangalore.
Member	Dr. R.D. Kulkarni, M.D. Consulting Physician, Clinical Pharmacology, 251, Dr. D.N. Road, Bombay.
Member	Dr. J.S. Guleria, M.D., D.M., F.A.M.S., F.N.C.C.P. Prof. & Head, Deptt. of Medicine University College of Medical Sciences and G.T.B. Hospital, Shahdara, Delhi.

Member	Commissioner Food & Drugs Control Administration Maharashtra State Bombay.
Member	Director Food & Drugs Control Administration Gujarat State Ahmedabad (Dr. M.A. Patel, M. Pharm., Ph.D.)
Member	Drugs Controller Karnataka Bangalore (Dr. V.B. Desai)
Member	Shri R.S. Iyer, M.Sc., M.Chem.A., F.R.S.C. Ex-Director, Corporate Quality Assurance M/s. Glaxo Laboratories (India) Limited 12, Kamakshipuram Layout, Anandnagar, Bangalore.
Member	Dr. G. Ramana Rao, M.Sc., Ph.D. Chief, Quality Control Department Indian Drugs and Pharmaceuticals Limited Hyderabad.
Member	Dr. Parvinder Singh, M.Pharm., Ph.D. Vice-Chairman & Managing Director M/s. Ranbaxy Laboratories Limited New Delhi.
Member	Director Central Drugs Laboratory, Calcutta (Dr. S.K. Roy, M.Sc., Ph.D., F.I.C.)
Member	Director Central Research Institute Kasauli (Dr. S.N. Saxena, M.B.B.S., M.D., Dip.Bact.)
Member	Director Central Indian Pharmacopoeia Laboratory Raj Nagar, Ghaziabad (Dr. P.D. Sethi, M.Pharm., Ph.D.)
Member-Secretary	Drugs Controller (India) Directorate General of Health Services Nirman Bhawan New Delhi (Dr. Prem K. Gupta, M.Pharm., Ph.D.)

As a part of the Supplement, the Committee brought out Addendum I to I.P. 1985 in 1989. The term of the Indian Pharmacopoeia Committee was extended upto 18th January, 1991, vide Govt. of India, Ministry of Health & Family Welfare Resolution No. X.19020/1/89-DMS&PFA dated 25th April, 1989 to complete its work.

Addendum II completes the remaining contents.

The Committee appointed the following Sub-committees:

1. *Clinical Medicine and Pharmacology Sub-committee*

   Dr. J.S. Guleria (Chairman), Dr. R.D. Kulkarni, Dr. P.L. Sharma, Dr. B.M. Hegde, Dr. K.V. Thiruvengadam.

2. *Biological Products & Bio-assay Sub-committee*

   Dr. S.N. Saxena (Chairman), Dr. V.R. Kalyanraman, Dr. M.B. Borkar, Dr. K.V. Jogi, Dr. A.G. Mulgaonkar, Dr. S.S. Chakravorti, Dr. Meera Savkar, Dr. Sharda Sharmugasundram, Dr. L.R. Sood, Dr. Y.P. Nanda, Dr. Shivedkar.

3. *Drug Substances Sub-committee*

   Dr. Parvinder Singh (Chairman), Dr. G. Ramana Rao, Dr. S.K. Roy, Dr. S.B. Phadke, Dr. Surabhai Shah, Dr. S. Dayal, Dr. R.S. Kapil, Dr. Harkishan Singh.

4. *Dosage Forms Sub-committee*

   Shri R.S. Iyer (Chairman), Shri R.N. Dhar, Dr. P.D. Sethi, Dr. R.C. Mehta, Dr. P. Ramanujam, Shri P.D. Sheth, Dr. A.C. Das Gupta, Dr. A.D. Nadkarni.

5. *Chemical and Pharmaceutical Aids Sub-committee*

   Dr. G. Ramana Rao (Chairman), Dr. J.L. Sipahimalani, Shri Santosh Yellore, Dr. A.G. Mulgaonkar, Dr. T.R. Tyagarajan, Dr. H.P. Tipnis, Shri V. Subramony.

6. *Medical Devices Sub-committee*

   Dr. M.A. Patel (Chairman), Dr. K.R. Baghat, Dr. P.C. Shah, Dr. H.V. Shah, Dr. N.G.S. Gopal.

7. *Medicinal Plants, Natural Products and Galenicals Sub-committee*

   Dr. M.A. Patel (Chairman), Dr. R.T. Sane, Dr. B.N. Dhawan, Dr. G.V. Satyawati, Shri G.G. Parikh, Kum. S. Satkopan.

8. *Analytical Methods Sub-committee*

   Dr. S.K. Roy (Chairman), Dr. P.D. Sethi, Dr. A.D. Nadkarni, Shri J.P. Ganatra, Dr. M.K. Mazumdar, Dr. S.N. Mahajan, Dr. R.C. Mahajan.

9. *Radio Pharmaceuticals Sub-committee*

   Dr. R.D. Kulkarni (Chairman), Shri S.D. Bhirud, Dr. R.S. Mani, Dr. R.D. Ganatra.

10. *Surgical Dressings Sub-committee*

    Shri S.S. Kattishetar (Chairman), Dr. S.N. Iyer, Dr. S.C. Madan, Sh. M.M. Deb.

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*Reconstituted on 6th May, 1988.

11. *Veterinary Drugs Sub-committee*

Dr. P.N. Bhat (Chairman), Dr. J.N. Dwivedi, Shri V. Subramony, Dr. P.P. Jamkhedkar, Dr. Z. Mathew, and Heads, Divisions of Biological Products, Standardisation, Pharmacology & Toxicology, Indian Veterinary Research Institute, Izatnagar.

In order to expedite the preparation of Addendum II to the Indian Pharmacopoeia, the I.P. Committee reconstituted its Working Group for preparing the draft monographs and appendices, to examine the comments received on these and to make suitable recommendations thereon to the Committee. The Composition of the Working Group is as under:—

(Effective from 23rd March, 1984 to 3rd November, 1989)
Dr. A.D. Nadkarni (Chairman), Dr. R.C. Mehta, Shri R.S. Iyer, Dr. Ajit Dangi, Dr. Parvinder Singh.

(Reconstituted on 3rd November, 1989 till 18th January, 1991)
Dr. parvinder Singh (Chairman), Shri R.S. Iyer, Dr. Anand Prabhu, Dr. P. Ramanujam, Dr. A.G. Shah, Dr. P.R. Pabrai.

Acknowledgements

The Indian Pharmacopoeia Committee takes this opportunity to place on record its appreciation of the services rendered by the staff of the Committee and the Research & Development wing of Central Indian Pharmacopoeia Laboratory, Ghaziabad in the preparation of Addendum (II).

The Committee acknowledges with gratitude the valuable contribution made by the members of the sub-committees and the working Groups, particularly Shri R.S. Iyer and Dr. P.R. Pabrai in the preparation of this Addendum.

The Committee also wishes to express its thanks to all those persons working in the drug control laboratories, research and teaching institutions and the pharmaceutical industry who have assisted the Committee in the compilation of Addendum II.

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Introduction

पुस्तकालय
पुस्तकालय
गुरुकुल कांगड़ी विश्वविद्यालय

The Third edition of Pharmacopoeia of India was published in 1985 followed by Addendum I to it in 1989. After the publication of the first Addendum a number of new drugs came into use necessitating the publication of another Addendum. A list of drugs commonly used but *not* included in the Indian Pharmacopoeia was drawn up by the Clinical Medicine & Pharmacology Sub-committee and approved by the I.P. Committee. The draft monographs were prepared by the Working Group and circulated widely for comments to members of the I.P. Committee, its concerned Sub-committees, manufacturers, Associations, Zonal Offices of Central Drugs Standard Control Organisation, etc. Comments received were examined by the Working Group and the finalised monographs were subsequently approved by the I.P. Committee.

The Addendum II adds to the Pharmacopoeia 62 new monographs and makes amendments to monographs and appendices currently official. The existing monographs on Activated Dimethicone, Oxytocin Injection and Povidone have been completely rewritten and therefore replace those in I.P., third edition. Notable new drugs included in this Addendum are the adrenergic (bronchodilator) Terbutaline Sulphate, local anaesthetic Bupivacaine Hydrochloride, analgesic, antipyretic and anti-inflammatory Propyphenazone, ß-receptor antagonist (antihypertensive, antianginal and antiarrhythmic) Metoprolol Tartrate, coronary vasodilator Nifedipine, antibacterial Framycetin Sulphate, heparin antagonist Protamine Sulphate, antiprotozoal Tinidazole, oxytocic Oxytocin, antiseptic Povidone-Iodine, replacement solution for diarrhoeal dehydration Oral Rehydration Salts and some important pharmaceutical aids including Alginic Acid, Hydrogenated Castor Oil, Caramel, Carnauba Wax, Cetyl Alcohol, Ethylcellulose, Hard Gelatin Capsule Shells, Hydroxypropylcellulose, Hydroxypropylmethylcellulose, Icing Sugar, Isopropyl Alcohol, Methylene Chloride, Monothioglycerol, Sodium Alginate, Sodium Formaldehyde Sulphoxylate, Sodium Starch Glycollate, Sodium Methylparaben, Sodium Propylparaben, Sorbic Acid, Stearyl Alcohol, Colloidal Silicon Dioxide and Microcrystalline Wax.

Preparations of substances referred to above are added, for example, Terbutaline Sulphate Injection and Tablets, Bupivacaine Injection, Povidone-Iodine Solution, Protamine Sulphate Injection, Nifedipine Capsules, Tinidazole Tablets, Oxytocin Nasal Solution, Metoprolol Tartrate Tablets.

Besides, several new preparations of substances already included in the Pharmacopoeia or its Addendum have also been included. For example, Betamethasone Inhaler, Betamethasone Valerate Ointment, Miconazole Ointment, Furazolidone Tablets, Pyrimethamine and Sulphadoxine Tablets, Ethosuximide Syrup, Paracetamol Syrup, Pheniramine Maleate Injection, Metronidazole Injection, Hydrocortisone Sodium Succinate Injection, Promethazine Syrup, Piperazine Citrate Syrup, Salbutamol Syrup, Sulphacetamide Eye Drops, Mannitol Injection, Metoclopramide Syrup, Metronidazole Benzoate Oral Suspension, Trimethoprim and Sulphamethoxazole Suspension and Chlorhexidine Gluconate Solution.

A new Appendix on the Biological Assay of Protamine Sulphate has been added as Appendix 2.43. Appendix 5.4.4 on High Performance Liquid Chromatography (HPLC) has also been introduced. With this technique high speed resolution with high sensitivity and reproducibility can be obtained and non-volatile and thermolabile compounds can be analysed directly. Appendix 5.20 on the Determination of Water by Azeotropic Distillation method required for Monothioglycerol has also been added.

ADDITIONS

The following monographs are added to the Indian Pharmacopoeia, 1985 by means of this Addendum:

Alginic Acid
Beclomethasone Inhaler
Beclomethasone Valerate Ointment
Bupivacaine Hydrochloride
Bupivacaine Injection
Hydrogenated Caster Oil
Caramel
Carnauba Wax
Cetyl Alcohol
Chlorhexidine Gluconate Solution
Ethosuximide Syrup
Ethylcellulose
Framycetin Sulphate
Furazolidone Tablets
Hard Gelatin Capsule Shells
Hydrocortisone Sodium Succinate Injection
Hydroxypropylcellulose
Hydroxypropylmethylcellulose
Icing Sugar
Isopropyl Alcohol
Mannitol Injection
Methylcellulose
Methylene Chloride
Metoclopramide Syrup
Metoprolol Tartrate
Metoprolol Tartrate Tablets
Metronidazole Benzoate Oral Suspension
Metronidazole Injection
Miconazole Ointment
Monothioglycerol
Nifedipine
Nifedipine Capsules
Oral Rehydration Salts
Oxytocin
Oxytocin Nasal Solution
Paracetamol Syrup
Pheniramine Maleate Injection
Piperazine Citrate Syrup
Povidone-Iodine
Povidone-Iodine Solution
Promethazine Syrup
Propyphenazone

ADDITIONS (contd.)

Protamine Sulphate
Protamine Sulphate Injection
Pyrimethamine and Suphadoxine Tablets
Salbutamol Syrup
Colloidal Silicon Dioxide
Sodium Alginate
Sodium Formaldehyde Sulphoxylate
Sodium Methylparaben
Sodium Propylparaben
Sodium Starch Glycollate
Sorbic Acid
Stearyl Alcohol
Sulphacetamide Eye Drops
Terbutaline Sulphate
Terbutaline Injection
Terbutaline Tablets
Tinidazole
Tinidazole Tablets
Trimethoprim and Sulphamethoxazole Suspension.
Microcrystalline Wax

AMENDMENTS

The following monographs of the Indian Pharmacopoeia, 1985 and Addendum (I) are amended by this Addendum:

Absorbent Lint
Human Normal Serum Albumin
Alcohol
Aluminium Hydroxide
Aluminium Hydroxide Tablets
Aminophylline Injection
Ampicillin Injection
Ampicillin for Oral Suspension
Betamethasone Tablets
Betamethasone Sodium Phosphate Tablets
Whole Human Blood
Caffeine
Calcium Carbonate
Calcium Gluconate
Tribasic Calcium Phosphate
Castor Oil
Microcrystalline Cellulose
Cephaloridine Injection
Chloramphenicol
Chloramphenicol Capsules
Chloroform Spirit
Chlorpheniramine Tablets
Chlorpromazine Hydrochloride
Chlorpromazine Tablets
Clonidine Injection
Clotrimazole
Absorbent Cotton Wool
Cyclophosphamide Injection
Dexamethasone Sodium Phosphate Injection

AMENDMENTS (contd.)

Dextropropoxyphene Capsules
Dextrose
Dextrose Injection
Diloxanide Furoate
Activated Dimethicone
Anaesthetic Ether
Eye Ointments
Folic Acid Tablets
Dried Human Antihaemophilic Fraction
Gelatin
Gentamycin Sulphate
Human Normal Immunoglobulin
Dried Human Normal Immunoglobulin
Glycerin
Griseofulvin
Hydrocortisone Eye Ointment
Ibuprofen Tablets
Injections
Iron Dextran Injection
Heavy Kaolin
Light Kaolin
Lignocaine Hydrochloride Injection
Heavy Magnesium Oxide
Magnesium Trisilicate
Mebendazole Tablets
Mephenteramine Injection
Mercaptopurine Tablets
Metformin Tablets
Methdilazine Hydrochloride
Methyldopa
Methylparaben
Metoclopropamide Injection
Metronidazole Benzoate
Naproxen
Nitrous Oxide
Nystatin
Oxygen
Oxyphenbutazone
Oxyphenbutazone Tablets
Oxytetracycline Hydrochloride
Oxytetracycline Injection
Oxytocin Injection
Paracetamol
Pentazocine
Pentazocine Injection
Pheniramine Tablets
Phenoxymethylpenicillin Potassium Tablets
Phenylbutazone Tablets
Piperazine Adipate Tablets
Human Plasma Protein Fraction
Polyethylene Glycol 6000
Polyvinylpyrrolidone
Potassium Citrate
Prochlorperazine Maleate

AMENDMENTS (contd.)

Prochlorperazine Tablets
Propantheline Tablets
Propranolol Injection
Salbutamol
Salbutamol Injection
Salbutamol Sulphate
Salbutamol Tablets
Sodium Carboxymethylcellulose
Senna Fruit
Compound Sodium Lactate Injection
Sodium Phosphate
Spironolactone
Spironolactone Tablets
Succinylcholine Chloride Injection
Sulphacetamide Sodium
Sulphacetamide Eye Ointment
Tetracycline Hydrochloride
Thiamine Hydrochloride
Thiopentone Injection
Thyroid
Titanium Dioxide
Trifluoperazine Hydrochloride
Trifluoperazine Tablets
Triflupromazine Hydrochloride
Triflupromazine Tablets
Vitamin A
Sterile Water for Injection

The contents of Addendum II have been page-numbered in continuation of Addendum I. Thus the amendments to monographs have been page-numbered starting from page 63 onwards and the appendices have been page-numbered starting from A-13 onwards. The Index in Addendum II is a combined Index for Addendum I and Addendum II, and should be referred to accordingly.

Amendments to the Monographs

I.P. Third Edition

General Notices
Page 10

Line 10
For 'to a powder'
read 'to a *fine powder*'

Human Normal Serum Albumin
Page 22

Standards—Line 7
For 'hepatitis B surface antigen'
read 'hepatitis B surface antigen and HIV antibodies'

Alcohol
Page 24

Fuel oil constituents
Change the statement to:
Place 25 ml in a porcelain dish protected from dust and allow the liquid to evaporate on a water-bath until a little of the liquid remains. Remove the dish from the water-bath and allow the liquid in the dish to evaporate at room temperature till the dish is almost dry. No foreign odour is perceptible. Add 1 ml of *sulphuric acid;* no red or brown colour is produced.

Aluminium Hydroxide Gel
Page 26

Neutralising capacity—Line 7
For '4.0'
read '4.5'

Aluminium Hydroxide Tablets
Page 27

Neutralising capacity
Change the statement to:
Pass a sufficient quantity of the powder prepared for use in the **Assay** through a sieve of nominal mesh aperture 150 µm. Weigh accurately a quantity of the powder equivalent to 0.5 g of Dried Aluminium Hydroxide Gel, mix with a small quantity of *water* to give a smooth paste and slowly add further quantities of *water* to a total volume of 100.0 ml. Warm to 37°, add 100.0 ml of *0.1N hydrochloric acid* previously heated to 37°, and stir continuously, maintaining the temperature at 37°; pH of the solution at 37°, after ten, fifteen and twenty minutes, is not less than 1.6, 1.8 and 2.2 respectively, and at no time is more than 4.0. Add 10.0 ml of *0.5N hydrochloric acid* previously heated to 37°, stir continuously for one hour, maintaining the temperature at 37°, and titrate the solution with *0.1N sodium hydroxide* to pH 3.5. The volume of *0.1N hydrochloric acid* consumed is not less than 115 ml.

Aminophylline Injection
Page 31

Standards— Line 6
For '102.0 per cent'
read '107.0 per cent'

Ampicilline for Oral Suspension
Page 40

Water—Line 1
For '2.5 per cent w/w'
read '5.0 per cent w/w'

Assay—Lines 1 to 3
Delete the statement 'however, the result obtained frcm the microbiological assay shall be official.'

Stability of suspension—Line 5
For '90.0 per cent'
read '80.0 per cent'

Ampicillin Injection
Page 41

Standards: Add the following as second paragraph:

'Ampicillin Injection contains a quantity of Ampicillin Sodium equivalent to not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of ampicillin, $C_{16}H_{19}N_3O_4S$.'

Content of ampicillin, $C_{16}H_{19}N_3O_4S$.
Delete the statement.

Assay
Change the statement to:
'Determine the weight of the contents of ten containers and carry out the **Assay** described under Ampicillin Sodium, using 0.12 g of the mixed contents.'

Betamethasone Tablets
Page 70

Uniformity of content—Lines 12 to 15
For 'The content .... of the average.'
read 'The content of each tablet is between 85 and 115 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.'

Betamethasone Sodium Phosphate Tablets
Page 72

Uniformity of content—Lines 11 to 14
For 'The content .... of the average'.
read 'The content of each tablet is between 85 and 115 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.'

Whole Human Blood
Page 77

Standards—Line 20
For 'evidence of syphilitic infection.'
read 'syphilitic infection and HIV antibodies.'

Caffeine
Page 81

Alkaloids
Change the statement to:
To 5 ml of a 2 per cent w/v solution add a few drops of *potassium mercuric-iodide solution;* no precipitate is formed.

Calcium Carbonate
Page 84

Sulphate—Line 1
For '0.5 g'
read '0.25 g'

Calcium Gluconate
Page 85

Standards
Change the statement to:
Calcium Gluconate contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{12}H_{22}CaO_{14}$, calculated with reference to the dried substance.

After the test for **Sucrose and reducing sugars** add the following:
Loss on drying: Not more than 6.5 per cent, determined on 0.5 g, finely powdered, by drying "in vacuo at 110°", Appendix 5.8.

Tribasic Calcium Phosphate
Page 90

Acid-insoluble substances—Line 1
For '0.2 per cent'
read '0.3 per cent'

Castor Oil
Page 95

Water
Delete the test

Microcrystalline Cellulose
Page 96

Identification: (B)—Lines 3 and 4
For *'dilute sulphuric acid'*
read *'sulphuric acid (66 per cent v/v)'*

Cephaloridine Injection
Page 100

Storage—Lines 1 and 2
For 'at a temperature not exceeding 15°'
read 'in a cool, dry place.'

Chloramphenicol
Page 103

After **Assay** change the statement to:
Chloramphenicol intended for parenteral administration or for the preparation of eye drops without further sterilisation complies with the following additional requirements:

Chloramphenicol Capsules
Page 103

Identification; Melting range; Specific optical rotation—Line 4
For *'light petroleum (boiling range, about 120°)'*
read *'light petroleum (boiling range, 60° to 80°)*
or. light petroleum (boiling range, 100° to 120°)'

Chloroform Spirit
Page 111

Delete the monograph.

Chlorpheniramine Tablets
Page 117

Identification: (A)
Delete the test.

Identification: (B)
For '50 mg'
read '5 mg'

Chlorpromazine Hydrochloride
Page 118

pH—Line 1
For '4.0 and 5.0'
read '3.5 and 4.5'

Chlorpromazine Tablets
Page 119

Identification: (B)—Line 1
For 'test (B)'
read 'test (A)'

Line 5
For '0.5 mg'
read '5 mg'

Absorbent Cotton Wool
Page 138

Description—Line 1
For 'carded'
read 'well-carded'

Identification—Line 4
For 'matter'
read 'wall'

Acidity or Alkalinity—Line 2
For 'dosed'
read 'closed'

Cyclophosphamide Injection
Page 145

Assay: *For NaCl*
Change the statement to:
To an accurately measured volume equivalent to about 0.1 g of *sodium chloride* diluted, if necessary, to about 50 ml add 50.0 ml of *0.1N silver nitrate,* 3 ml of *nitric acid,* 5 ml of *nitrobenzene,* 2 ml of *ferric ammonium sulphate solution* and shake well. Titrate with *0.1N ammonium thiocyanate* until a reddish-yellow colour is produced. Each ml of *0.1N silver nitrate* is equivalent to 0.005844 g of NaCl.

Dexamethasone Sodium Phosphate Injection
Page 158

Identification—Line 14
For *'alkaline phosphate solution'*
read *'alkaline phosphatase solution'*

Dextrose
Page 161

Specific optical rotation—Line 1
For '+ 53.0°'
read '+ 53.3°'

Dextrose Injection
Page 162

pH
Change the statement to:
'Between 3.5 and 6.5, Appendix 5.10, when determined on a solution diluted, if necessary, with *carbon dioxide-free water* to a concentration of not more than 5 per cent w/v of dextrose, $C_6H_{12}O_6$ and to which 0.30 ml of saturated solution of *potassium chloride* has been added for each 100 ml of solution'.

Diloxanide Furoate
Page 173

Solubility—Line 2
For 'in *alcohol,* in *chloroform* and in *solvent ether'*
read 'in *alcohol* and in *chloroform;* slightly soluble in *solvent ether.'*

Activated Dimethicone
Page 177

Change the monograph to revised monograph.

Anaesthetic Ether
Page 199

Boiling range
For '34° and 36°'
read '34° and 35°'

Specific gravity
For '0.713 and 0.716'
read '0.714 and 0.716 at 20°'

Acetone and aldehyde—Line 6
After 'five minutes'
insert 'protected from light'

Eye Ointments
Page 209

Requirements of Tests
2. Particle size
Change the statement to:

Gently spread an accurately weighed small quantity of the ointment as a uniform thin layer on a microscope slide in such a way that an area of 1 sq mm of the slide represents about 25 µg of the ointment. Scan under a microscope at least 50 representative fields. Not more than ten particles have a maximum dimension greater than 50 µm and none has a maximum dimension greater than 100 µm for an area corresponding to 10 µg of the active ingredient.

Folic Acid Tablets
Page 222

Free amines
Delete the test

Dried Human Antihaemophilic Fraction
Page 222

Standards—Line 15
After 'haemagglutination'
delete 'and'

Line 16
After 'per cent w/v'
add ',and (e) whose blood has been tested with negative results for HIV antibodies by a sensitive method.'

Gelatin
Page 229

Microbial limits—Line 1
For 'Total bacterial count'
read 'Total microbial count'

Gentamicin Sulphate
Page 230

Identification: (B)
Change the statement to:

Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and as the mobile phase, the lower layer obtained by shaking together equal volumes of *strong ammonia solution*, *chloroform* and *methyl alcohol* and allowing to separate. Apply separately to the plate 10 µl of each of two solutions containing

(1) 0.5 per cent w/v of the substance being examined and (2) 0.5 per cent w/v of *gentamcin sulphate R.S.* After removal of the plate, allow it to dry in air, spray with a solution prepared by dissolving 1 g of *ninhydrin* in 50 ml of *alcohol* and adding 10 ml of *glacial acetic acid,* and heat at 110^0 for 5 minutes. The three principal spots in the chromatogram obtained with solution (1) correspond to the three principal spots in the chromatogram obtained with solution (2).

Human Normal Immunoglobulin
Page 233

Standards—Para 2, Line 10
For 'or any other infection.'
read 'or HIV or any other infection'

Dried Human Normal Immunoglobulin
Page 234

Standards—Line 3
After the words '.......... freeze-drying.'
insert the following:
The pool of immunoglobulin shall be tested for hepatitis B surface antigen and for HIV antibodies by suitable sensitive methods and shall show negative results in both cases.

Glycerin
Page 234

Wt. per ml
Change the statement to:
Between 1.252 g and 1.257 g, Appendix 5.19.

After **Sulphated ash** add the following:
Assay: Weigh accurately about 0.1 g, mix with 45 ml of *water,* add 25.0 ml of a 2.14 per cent w/v solution of *sodium periodate* and 1.0 ml of *2N sulphuric acid* and allow to stand for 15 minutes in the dark or in subdued light. Add 5 ml of a 50 per cent w/v solution of *ethylene glycol* and titrate with *0.1N sodium hydroxide,* using 0.5 ml of *dilute phenolphthalein solution* as indicator. Repeat the procedure without the substance being examined. The difference between the titrations represents the amount of sodium hydroxide required by the test substance. Each ml of *0.1N sodium hydroxide* is equivalent to 0.00921 g of $C_3H_8O_3$.

Griseofulvin
Page 236

Clarity and colour of solution
Change the statement to:
A 7.5 per cent w/v solution in *dimethylformamide* is clear and not more intensely coloured than a mixture of 6.0 ml of *ferric chloride C.S.,* 1.5 ml of *cobalt chloride C.S.* and 92.5 ml of *hydrochloric acid (1 per cent w/v).*

Hydrocortisone Eye Ointment
Page 247

Usual strength
For 'w/v'
read 'w/w'

Ibuprofen Tablets
Page 251

Assay—Line 3
After '*chloroform*'
add 'for 15 minutes,'

Injections
Page 256

Preparation of injections
4. Containers— Para 6, lines 2-3
For *'Glass Container for Injectable Preparation'*
read *'Glass Containers for Injectable Preparations'*

Iron Dextran Injection
Page 265

Dose
Change the statement to:
By intravenous or deep intramuscular injection, 1 to 2 ml daily or according to the needs of the patient.

Heavy Kaolin
Page 276

Lead
Delete the test and insert the following:

Heavy metals: Not more than 20 parts per million, determined by the following method. Heat 2.5 g for 15 minutes under a reflux condenser in a water-bath with a mixture of 35 ml of *water* and 5 ml of *hydrochloric acid* and filter. To 20 ml of the filtrate add 0.5 ml of *nitric acid* and evaporate to a low bulk. Add 20 ml of *water*, 2 g of *ammonium chloride* and 2 g of *ammonium thiocyanate* and extract with two quantities, each of 10 ml, of a mixture of equal volumes of *amyl alcohol* and *solvent ether.* To the aqueous layer add 2 g of *citric acid* and sufficient *water* to produce 50 ml. To 10 ml of the resulting solution add 2 ml of *acetate buffer, pH 3.5*, mix, add 1.2 ml of *thioacetamide reagent* and allow to stand for ten minutes. Any brown colour produced is not more intense than that obtained by treating in the same manner 5.0 ml of *dilute standard lead solution.*

Chloride—Line 3
For '50 ml'
read '10 ml'

Light Kaolin
Page 276

Identification; Alkaline or Acid impurities; Arsenic; Lead; Chloride; Iron; Loss on ignition
For **'Lead'**
read **'Heavy metals'**

Delete **'Chloride'** from the title and insert the following test:
Chloride: Boil 1.5 g with 40 ml of *water* and 10 ml of *dilute nitric acid* under a reflux condenser for five minutes, cool and filter. 50 ml of the filtrate complies with the *limit test for chlorides, Appendix 3.2.2.*

Coarse particles—Line 2
For '16 mm'
read '16 cm'

Heavy Magnesium Oxide
Page 291

Chloride—Line 1
For '0.4 g'
read '0.2 g'

Magnesium Trisilicate
Page 293

Heavy metals—Line 1
For '30 parts'
read '40 parts'
Line 2
For '2 g'
read '1.5 g'

Mebendazole Tablets
Page 296

Identification
Change the statement to:
Carry out the test for **Related substances** using for solution (2) a 0.5 per cent w / v solution of *mebendazole R.S.* in a mixture of 1 volume of *anyhydrous formic acid* and 9 volumes of *chloroform.* The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Assay
Change the statement to:
Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 50 mg of Mebendazole, add 50 ml of *0.5N methanolic hydrochloric acid* and shake for 30 minutes. Filter and discard the first 10 ml of the filtrate. Dilute 5.0 ml of the filtrate to 50.0 ml with *0.5N methanolic hydrochloric acid* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 234 nm, using *0.5N methanolic hydrochloric acid* as the blank. Calculate the content of $C_{16}H_{13}N_3O_3$ from the *extinction* obtained by repeating the operation using *mebendazole R.S.* in place of the substance being examined and from the declared content of $C_{16}H_{13}N_3O_3$ in the *mebendazole R.S.*

Mephenteramine Injection
Page 303

Assay—Line 7
For '0.008163 g'
read '0.01633 g'

Methdilazine Hydrochloride
Page 311

Assay—Line 3
For '100–ml'
read '1000–ml'

Methyldopa
Page 315

Heavy metals—Line 2
For 'Method A'
read 'Method B'

Methylparaben
Page 318

Solubility
Change the statement to:
Very slightly soluble in *water*; slightly soluble in *benzene* and in *carbon tetrachloride;* freely soluble in *alcohol* and in *solvent ether.*

Metronidazole Benzoate
Page 320

Melting range
For '100° and 102°'
read '98° and 102°'

Nitrous Oxide
Page 338

Nitric oxide and nitrogen dioxide
Change the statement to:
Not more than 5 parts per million in both the liquid and gaseous phases, determined by the following method. Use two cylinders of the type described in the test for **Acidity**, connected in series. Examine separately both the liquid and gaseous phases. To obtain the liquid phase, invert the cylinder. The liquid vaporises on leaving the valve. Dissolve 1 g of *sulphanilic acid* in a mixture of 10 ml of *glacial acetic acid* and 180 ml of *water* (solution 1). Dissolve 0.2 g of *N-(1-naphthyl)ethylenediamine hydrochloride* in 10 ml of a 50 per cent v / v solution of *glacial acetic acid*, heat gently, and dilute to 200 ml with *water* (solution 2). Mix 9 volumes of solution (1) with 1 volume of solution (2). Introduce 20 ml of this reagent mixture into one of the cylinders and connect the inlet tube of this cylinder to the outlet tube of the other cylinder containing a solution of 2.5 per cent w / v of *potassium permanganate* and 1.2 per cent w / v of *sulphuric acid.* Pass 2.5 litres of the gas being examined through the cylinders at a rate of 15 litres per hour. Prepare a reference solution by adding 0.25 ml of a 0.00308 per cent w / v solution of *sodium nitrite* to 20 ml of the reagent mixture. Allow both the sample solution and reference solution to stand for 10 minutes. For both the liquid and gaseous phases, any red colour in the sample solution is not more intense than that in the reference solution.

Nystatin
Page 343

Undue toxicity
Delete the title and statement.

After **Assay** add the following:
Nystatin intended for oral administration complies with the following additional requirement:

Undue toxicity: Complies with the test described under Bacitracin, using a quantity equivalent to not less than 600 Units suspended in not more than 0.5 ml of a 0.5 per cent w / v solution of *acacia* and injecting the suspension intraperitoneally.

Oxygen
Page 350

Assay
Change the statement to:
Carry out the *assay of oxygen*, Appendix 3.3.8, using 100 ml of oxygen and placing spirals of freshly cleaned copper wire and 125 ml of *ammonia buffer pH 10.9* in the pipette. The volume of the residual gas in the burette is not more than 1.0 ml.

Oxyphenbutazone
Page 351

After the test for **Heavy metals** add the following:
Related substances: Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel HF 254* as the coating substance and a mixture of 80 volumes of *chloroform* and 20 volumes of *glacial acetic acid* containing 0.02 per cent w / v of *butylated hydroxytoluene* as the mobile phase. Prepare the plate by allowing the solvent front to ascend

4 cm, remove the plate and dry it in a current of cold air for one minute. Without delay and under a current of nitrogen apply separately to the plate 5 µl of each of the following solutions prepared immediately before use. For solution (1) dissolve 0.1 g in 5 ml of a solution containing 0.02 per cent w/v of *butylated hydroxytoluene* in *ethyl alcohol*. For solution (2) dilute 1 ml of solution (1) to 200 ml with the ethanolic butylated hydroxytoluene solution. Develop immediately, allowing the solvent front to ascend 10 cm above the line of application. After removal of the plate, allow it to dry in a current of cold air for 15 minutes and examine under an ultraviolet lamp having a maximum output at about 254 nm. Any secondary spot in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (2).

Oxyphenbutazone Tablets
Page 351

Assay—Line 1
For 'Weigh and powder 20 tablets'
read 'Weigh 20 tablets and reduce to a *fine powder*'

Oxytetracycline Injection
Page 354

Labelling—Line 5
Change the statement (5) to:
the names of any preservatives used.

Oxytetracycline Hydrochloride
Page 355

After Assay change the statement to:
Oxytetracycline Hydrochloride intended for parenteral administration or for the preparation of Eye Ointments without further sterilisation complies with the following additional requirements:

Oxytetracycline Hydrochloride Injection
Page 356

Standards—Line 2
For 'Oxytetracycline'
read 'Oxytetracycline Hydrochloride'

Page 357

Labelling—Line 3
For 'contains'
read 'contained'

Line 4
For 'chlortetracycline'
read 'oxytetracycline'

Oxytocin Injection
Page 357

Change the monograph to revised monograph.

Paracetamol
Page 359

Melting range—Line 1
For '169°'
read '168°'

pH—Line 1
For '5.3'
read '5.1'

Pheniramine Tablets
Page 379

Assay
Change the statement to:
Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 45 mg of Pheniramine Maleate, shake with 20 ml of *0.1N hydrochloric acid* and centrifuge and transfer the supernatant liquid to a 100-ml volumetric flask. Repeat the extraction with three further quantities, each of 20 ml, of *0.1N hydrochloric acid*. Combine the extracts and add sufficient *0.1N hydrochloric acid* to produce 100.0 ml. Dilute 5.0 ml to 100.0 ml with *0.1N hydrochloric acid* and mix, measure and *extinction* of a 1-cm layer of the resulting solution at the maximum at about 265 nm, Appendix 5.15A, using *0.1N hydrochloric acid* as the blank. Calculate the content of $C_{16}H_{20}N_2,C_4H_4O_4$, taking 210 as the value of **E** (1 per cent, 1-cm) at the maximum at about 265 nm.

Phenoxymethylpenicillin Potassium Tablets
Page 383

Assay—Line 7
Add the following:
'and using *phenoxymethylpenicillin R.S.* in place of *benzylpenicillin sodium R.S.*'

Phenylbutazone Tablets
Page 386

Assay
Change the statement to:
Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.5 g of Phenylbutazone and shake vigorously for about 45 minutes with 150 ml of *0.1N sodium hydroxide*. Add sufficient *0.1N sodium hydroxide* to produce 250.0 ml, mix and filter, rejecting the first 20 ml of the filtrate. To 5.0 ml of the filtrate add 50 ml of *water* and 4 ml of *hydrochloric acid.* Extract with three quantities, each of 30 ml, of *solvent ether,* combine the ether extracts and extract with three quantities, each of 30 ml, of *0.1N sodium hydroxide*. Combine the aqueous extracts, aerate the solution with nitrogen to remove residual ether, add sufficient *0.1N sodium hydroxide* to produce 100.0 ml and mix. To 10.0 ml add sufficient *water* to produce 100.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 264 nm, using *0.1N sodium hydroxide* as the blank, Appendix 5.15A. Calculate the content of $C_{19}H_{20}N_2O_2$ from the *extinction* obtained by carrying out the assay simultaneously on 0.5 g of *phenylbutazone R.S.* and from the declared content of $C_{19}H_{20}N_2O_2$ in the *phenylbutazone R.S.*

Piperazine Adipate Tablets
Page 394

Assay—Line 6
For '*sulphuric acid*'
read '*2 N sulphuric acid*'

Piperazine Hydrate
Page 395

Identification
Add the following:
(C) It melts at about 42^0, Appendix 5.11.

Melting range
Delete the title and statement.

Human Plasma Protein Fraction
Page 398

Standards—Line 15
After the words '.... obtained' insert the following:
It shall be tested for hepatitis B surface antigen and for HIV antibodies by suitable sensitive methods and shall show negative results in both cases.

Polyethylene Glycol 6000
Page 401

Standards—Line 4
For 'between 158 and 204'
read 'between 112 and 158'

Lines 4, 5 and 6
For 'It has an average weight of not less than 7000 and not more than 9000'
read 'It has an average molecular weight of not less than 5000 and not more than 7000'

Congealing range
For '63°'
read '60°'

Viscosity—Line 1
For '470 cs and 900 cs'
read '250 cs and 390 cs'

Polyvinylpyrrolidone
Page 403

Change the monograph to revised monograph entitled 'POVIDONE'

Potassium Citrate
Page 405

Readily carbonisable substances—Line 1
For '1.0 g'
read '0.2 g'

Prochlorperazine Maleate
Page 417

Identification (D)
Change the statement to:
Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and mixture of 5 volumes of *ethyl acetate*, 3 volumes of *methyl alcohol*, and 2 volumes of *dilute acetic acid*, as the mobile phase. Apply separately to the plate 5 µl of each of the following two solutions in a mixture of equal volumes of *methyl alcohol* and *chloroform* containing (1) 0.1 per cent w/v of the substance being examined; and (2) 0.1 per cent w/v of *prochlorperazine maleate R.S.* After removal of the plate, allow it to dry in air and examine under ultra-violet lamp having a maximum output at about 254 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Prochlorperazine Tablets
Page 419

Assay—Line 5
For '0.01 per cent v/v'
read '1.0 per cent v/v'

Salbutamol Sulphate
Page 450

Category
Change the statement to:
Bronchodilator (beta-adrenoceptor stimulant).

Page 451

Identification: (B)
Change the statement to:
To 2 ml of a 1 per cent w / v solution add 0.1 ml of *ferric chloride test solution*; a violet colour develops which on addition of 1 ml of *sodium bicarbonate solution* changes to orange and the solution may become opalescent.

Foreign substances
Change the title to:
Related substances

Lines 9 and 10
For *'1-(4-hydroxy-3-methylphenyl)-2-(butylamino)ethanol R.S.'*
read *'salbutamol sulphate R.S.'*

Salbutamol Tablets
Page 451

Category
Change the statement to:
Bronchodilator (beta-adrenoceptor stimulant).

Uniformity of content—Line 2
For 'basic anion exchange resin'
read 'basic anion exchange resin (Amberlite resin IRA-410 is suitable)'

Senna Fruit
Page 456

Assay—Line 13
For 'until the precipitate is dissolved'
read 'add 1.0 ml of *hydrochloric acid*, shake well and continue heating under reflux for another 20 minutes until the precipitate is dissolved'

Sodium Carboxymethylcellulose
Page 467

Heavy metals
Change the statement to:
Not more than 40 parts per million, determined by Method B, Appendix 3.2.4, using a test solution prepared in the following manner. Weigh 0.5 g into a suitable crucible, add sufficient *sulphuric acid* to wet the substance, and carefully ignite at a low temperature until thoroughly charred. Add to the carbonised mass 2 ml of *nitric acid* and 5 drops of *sulphuric acid*, and heat cautiously until white fumes are no longer evolved. Ignite, preferably in a muffle furnace, at 500° to 600°, until the carbon is completely burnt off. Cool, and add 4 ml of *6N hydrochloric acid*, cover, digest on a water-bath for 15 minutes, uncover, and slowly evaporate on a water-bath to dryness. Moisten the residue with one drop of *hydrochloric acid*, add 10 ml of hot *water* and 1 ml of a 20 per cent w / v solution of *hydroxylamine hydrochloride* and digest for two minutes. Filter, if necessary, and add sufficient *water* to produce 25 ml.

Compound Sodium Lactate Injection
Page 474

Standards
Delete lines 9 to 27.

Sodium Phosphate
Page 476

Monosodium phosphate
Change the statement to:
The value of the expression $(n_2-n)/(n-n_1)$, where n, n_1 and n_2 are the titres of *N sodium hydroxide* obtained in the **Assay**, does not exceed 0.05.

Assay
Change the statement to:
Weigh accurately about 4 g (w g), dissolve in 25.0 ml of *water*, and add 25.0 ml of *N hydrochloric acid* and titrate potentiometrically with *N sodium hydroxide* until pH 4.4 is reached (n_1 ml). Continue the titration until pH 9.2 is reached (n_2 ml). Titrate 25.0 ml of the *N hydrochloric acid* with *N sodium hydroxide* to pH 4.4 (n ml). Determine the percentage content of Na_2HPO_4 from the expression $1420(n-n_1)/w(100-d)$, where d is the percentage loss on drying.

Spironolactone
Page 480

Sulphur—Line 1
For '7.05 per cent'
read '7.95 per cent'

Succinylcholine Chloride Injection
Page 487

Storage—Line 2
For 'at a temperature not exceeding 4°'
read 'in cold place'

Sulphacetamide Sodium
Page 490

Loss on drying
Change the statement to:
Water: Between 6.0 per cent and 8.0 per cent, Appendix 3.3.25.

Sulphacetamide Eye Ointment
Page 490

Identification—Line 11
For 'tests (A) to (C)'
read 'tests (A) and (B)'
For 'Sulphacetamide'
read 'Sulphacetamide Sodium'

Tetracycline Hydrochloride
Page 508

After **Assay** change the statement to:
Tetracycline Hydrochloride intended for parenteral administration or for the preparation of eye drops without further sterilisation complies with the following additional requirements:

Thiopentone Injection
Page 518

Content of thiopentone $C_{11}H_{18}N_2O_2S$—Lines 4 to 7
For 'The weight......... 15 per cent'.
read 'From the result of the **Assay** calculate the proportionate amount of thiopentone, $C_{11}H_{18}N_2O_2S$, in each container. This amount does not deviate from the amount stated on the label by more than 10 per cent except that in one container the content may deviate by not more than 15 per cent'.

Thyroid
Page 519

Standards

Add the following at the end:

It may contain suitable harmless diluents such as Lactose, Sodium Chloride, Starch or Sucrose.

Titanium Dioxide
Page 523

Assay

Change the statement to :

Weigh accurately about 0.5 g, add 5 g of *anhydrous sodium sulphate* and 10 ml of *water*, mix and add 10 ml of *sulphuric acid.* Boil gently in a long-necked combustion flask until clear (about 25 minutes). Cool, add slowly 40 ml of cooled *sulphuric acid (25 per cent v/v)*, cool again and dilute with *water* to 100.0 ml (solution A). To 300 g of *granulated zinc* add 300 ml of a 2 per cent w/v solution of *mercuric nitrate* and 2 ml of *nitric acid*, shake for ten minutes and wash with *water.* Pack the amalgamated zinc into a glass tube (400 mm x 20 mm) fitted with a tap and a filter plate. Pass through the column 100 ml of *2N sulphuric acid* followed by 100 ml of *water*, ensuring that the amalgam is covered with liquid throughout. Pass slowly through the column, at a rate of about 3 ml per minute, 200 ml of *N sulphuric acid* followed by 100 ml of *water.* Collect the combined eluates in a flask containing 50.0 ml of a 15 per cent w/v solution of *ferric ammonium sulphate* in *sulphuric acid (25 per cent v/v)* and titrate immediately with *0.1N ceric ammonium nitrate*, using *ferroin sulphate solution* as indicator (T_1 ml). Pass slowly through the column 200 ml of *N sulphuric acid* followed by 20.0 ml of solution A, wash with 100 ml of *N sulphuric acid* followed by *water.* Collect the combined eluates in a flask containing 50.0 ml of a 15 per cent w/v solution of *ferric ammonium sulphate* in *sulphuric acid (25 per cent v/v)* and titrate immediately with *0.1N ceric ammonium nitrate*, using *ferroin sulphate solution* as indicator (T_2 ml). Calculate the percentage content of TiO_2 from the expression $3.99(T_2-T_1)/W$ where, W is the weight in g of the substance being examined taken to prepare solution A.

Trifluoperazine Hydrochloride
Page 529

Category

Change the statement to:

Antipsychotic (tranquillizer); antiemetic.

Dose

Change of statement to :

In psychiatric states, orally, the equivalent of 2 to 30 mg of trifluoperazine daily, in divided doses; by intramuscular injection, the equivalent of 1 to 2 mg of trifluoperazine every 4 to 6 hours, as required; as antiemetic, the equivalent of 1 to 6 mg of trifluoperazine daily.

Triflupromazine Hydrochloride
Page 529

Category

Change the statement to :

Antipsychotic (tranquillizer); antiemetic.

Dose

Change the statement to:

In psychiatric states, orally, initial dose, the equivalent of 100 to 150 mg of triflupromazine daily, in divided doses; maintenance dose, the equivalent of 30 to 150 mg of triflupromazine daily, in divided doses; as antiemetic, the equivalent of 20 to 30 mg of triflupromazine daily.

Vitamin A
Page 542

Identification: (B)—Line 8
For '50 Units'
read '50,000 Units'
Line 10
For '500 Units'
read '50,000 Units'
Line 18
For 'per ml'
read 'per μl'

Sterile Water for Injection
Page 545

Description

Delete the title and statement

After **Standards** add the following:

Description: Clear, colourless liquid; odourless.

Oxidisable substances—Line 2
For '0.2 ml'
read '0.4 ml'
Line 4
For '0.4 ml'
read '0.2 ml'

Other requirements

Add the following:

Complies with the requirements stated under Injections.

Addendum (I)
Notices
Page (v)

LEGAL NOTICES

Para 3, Lines 1 and 2
For 'Dangerous Drugs Act, 1930'
read 'Narcotic Drugs and Psychotropic Substances Act, 1985'

Preface
Page (vii)

Line 5
For 'Dangerous Drugs Act, 1930'
read 'Narcotic Drugs and Psychotropic Substances Act, 1985'

Introduction
Page (xv)

Para 4, Line 1
For 'Preparation'
read 'Preparations'
Para 5, Line 1
For 'Preparation'
read 'preparations'

Page (xvi)

Line 2
For 'Pharmacopoeia'
read 'the Pharmacopoeia'

Absorbent Lint
Page 13

Description—Line 4
Delete the amendment.

Standards—Line 2
Delete the amendment.

Thiamine Hydrochloride
Page 22

For **'Identification**—Line 2'
read **'Identification:** (C)—Line 2'

Clonidine Injection
Page 30

Dose
Change the statement to:
Clonidine Hydrochloride. By slow intravenous injection, 0.1 to 0.3 mg.

Clotrimazole
Page 31

Identification: (C)—Line 1
For '148°'
read '143°'

Dextropropoxyphene Capsules
Page 33

Identification—Line 3
For 'chloroform'
read '*chloroform*'
Test (A)—Line 1
For 'infra-red absorption spectrum'
read '*infra-red absorption spectrum*'
Assay—Line 16
Delete the word 'anhydrous'

Lignocaine Hydrochloride Injection
Page 42

Synonym
For 'Lingocaine'
read 'Lignocaine'

Mercaptopurine Tablets
Page 42

Category
Change the statement to :
'Antineoplastic'

Metformin Tablets
Page 42

Category
Change the statement to:
'Oral hypoglycaemic'

Metoclopramide Injection
Page 44

Identification: (A)—Lines 5 and 6
Add 'about' between 'at' and '273 nm'
Add 'about' between 'at' and '309 nm'

Naproxen
Page 46

Identification: (B)—Line 2
For '0.004 per cent'
read '0.002 per cent'

Pentazocine
Page 51

Standard —Line 1
For '(*2R, 6R, 11R*)'
read '(*2R**, *6R**, *11R**,)'

Identification: (C)—Line 4
For 'deeper slightly'
read 'slightly deeper'

Related substances—Last line
For 'additional spots'
read 'additional minor spots'

Assay—Line 1
For '6.0 g'
read '0.6 g'

Pentazocine Injection
Page 51

Dose
Change the statement to:
By subcutaneous, intramuscular, or intravenous injection, the equivalent of 30 to 60 mg of pentazocine, every three to four hours.

Propantheline Tablets
Page 55

Assay—Line 1
For '40 tablets'
read '20 tablets'
Line 12
For '*anhydrous glacial acetic acid*'
read '*glacial acetic acid*'

Propranolol Injection
Page 55

Dose
Change the statement to:
Propranolol Hydrochloride, by slow intravenous injection, 3 to 10 mg.

Category
Change the statement to:
Beta-adrenergic blocker (antihypertensive; antianginal; antiarrhythmic).

Salbutamol
Page 56

Identification: (A)—Line 2
For 'of a layer of 0.008 per cent'
read 'of a 1-cm layer of 0.008 per cent'
Line 3
add the word 'about' before '276 nm' at both places it occurs.

Salbutamol Injection

Page 58

Standard—Line 7
For 'not more than 110.0 per cent'
read 'not more than the equivalent of 110.0 per cent'

Identification: (A)—Line 6
For 'at 276 nm'
read 'at about 276 nm'

Page 59

Identification: (B)—Line 3
For '4-aminophenazone'
read 'aminopyrazolone'

Spironolactone Tablets

Page 59

Category
Change the statement to:
Aldosterone inhibitor (diuretic)

Identification: (A)—Line 6
After 'infra-red absorption spectrum'
insert 'of the chloroform solution'

Trifluoperazine Tablets

Page 60

Usual strength
Change the statement to:
Usual strengths—The equivalent of 1 mg and 5 mg of trifluoperazine.

Uniformity of content—Line 19
For '90 and 110 per cent'
read '85 and 115 per cent'

Line 21
For '85 and 115 per cent'
read '80 and 120 per cent'

Triflupromazine Tablets

Page 60

Dose
Change the statement to:
Triflupromazine Hydrochloride. In pyschiatric states, initial dose, the equivalent of 100 to 150 mg of triflupromazine daily; maintenance dose, the equivalent of 30 to 150 mg of triflupromazine daily, in divided doses; as an antiemetic, the equivalent of 20 to 30 mg of triflupromazine daily.

Page 61

Identification: (B)—Lines 2 and 3
For 'maximum at about 305 nm'
read 'maximum at about 255 nm'

Uniformity of content—Line 16
For '90 and 100 per cent'
read '85 and 115 per cent'

Line 18
For '85 and 115 per cent'
read '80 and 120 per cent'

Monographs

Alginic Acid

Polymannuronic Acid

Category: Pharmaceutical aid (viscosity increasing agent).

Description: White to yellowish-white, fibrous powder; odourless or almost odourless; tasteless.

Solubility: Insoluble in *water* and in organic solvents; soluble in solutions of alkalies.

Standards: Alginic Acid is a hydrophilic colloidal carbohydrate extracted with dilute alkali from various species of brown seaweeds (*Phaeophyceae).*

Identification: (A) To 5 ml of a 0.75 per cent w/v solution in *0.1N sodium hydroxide* add 1 ml of *calcium chloride solution;* a bulky, gelatinous precipitate is formed.

(B) To 5 ml of the solution obtained in test A add 1 ml of *4N sulphuric acid;* a heavy, gelatinous precipitate is formed.

(C) To about 5 mg in a test-tube add 5 ml of *water,* 1 ml of a freshly-prepared 1 per cent w/v solution of *1,3-naphthalenediol* in *alcohol,* and 5 ml of *hydrochloric acid.* Heat the mixture to boiling, boil gently for 3 minutes, cool to about 15°. Transfer the contents of the test-tube to a small separator with the aid of 5 ml of *water,* and extract with 15 ml of *isopropyl ether;* the isopropyl ether extract exhibits a deep purple colour which is more intense than that shown by a blank prepared in the same manner without the substance being examined.

pH: Between 1.5 and 3.5, determined in 3.0 per cent w/v dispersion in *water,* Appendix 5.10.

Arsenic: Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals: Not more than 40 parts per million, determined on 0.5 g by Method B, and using *nitric acid Sp.* in place of *sulphuric acid Sp.* to wet the sample, Appendix 3.2.4.

Microbial limits : 1 g meets the requirements of the test for the absence of *E.coli* and 10 g is free from *salmonellae,* Appendix 4.5.

Acid Value: Not less than 230, calculated with reference to the dried substance and determined in the following manner. Weigh accurately about 1 g and suspend in a mixture of 50 ml of *water* and 30 ml of a 4.4 per cent w/v solution of *calcium acetate.* Shake vigorously, allow the mixture to stand for one hour, add *phenolphthalein solution* and titrate the liberated acetic acid with *0.1N sodium hydroxide.* Perform a blank determination. Calculate the acid value from the expression 5.611(A-B)/W, in which A and B are the volumes, in ml, of *0.1N sodium hydroxide* consumed in the titrations of the test solution and blank respectively and W is the weight in g of the sample.

Ash: Not more than 4.0 per cent, determined on 0.5 g by Method II and igniting at a temperature of 800 ± 25°, Appendix 3.3.22.

Loss on drying: Not more than 15.0 per cent, determined on 1.0 g by drying in an oven at 105° for 4 hours, Appendix 5.8.

Storage: Store in tightly-closed containers.

Beclomethasone Inhaler

Beclomethasone Inhalation Aerosol

Category: Adrenocortical steroid (topical anti-inflammatory).

Dose: Beclomethasone Dipropionate. For an adult, 2 inhalations, each of 50 μg, 3 or 4 times a day or up to a maximum of 20 inhalations in 24 hours. For a child, 1 or 2 inhalations, each of 50 μg, 3 or 4 times a day up to a maximum of 10 inhalations in 24 hours.

Usual strength: 50 μg in each metered dose.

Standards: Beclomethasone Inhaler is a suspension of microfine Beclomethasone Dipropionate in a suitable mixture of aerosol propellants. It may contain a surfactant, stabilising agent or other pharmaceutical aids. It is packed in a pressurised container fitted with a special metered-dose valve. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Beclomethasone Dipropionate, $C_{28}H_{37}ClO_7$, and it delivers not less than 75.0 per cent and not more than 125.0 per cent of the stated amount per inhalation of Beclomethasone Dipropionate, $C_{28}H_{37}ClO_7$, through an oral inhalation actuator.

Identification: Complies with the test for *identification of steroids,* Appendix 3.3.11, using solvent II and mobile phase D. Apply separately to the plate 10 μl of the following solutions. For solution (1) remove the actuator from the pressurised container, shake container for about 30 seconds and place it inverted in a small beaker containing 2 ml of a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol*. Discharge 40 deliveries below the surface of the liquid and use the resulting solution. Solution (2) is a 0.05 per cent w/v solution of *beclomethasone dipropionate R.S.* in a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol*.

Unit spray content: *Apparatus*—A sampling vessel consisting of a 150-ml beaker in which a stainless steel base plate is placed to facilitate the discharge of the aerosol . The base plate has three legs and a central, circular indentation with a hole approximately 1.5 mm in diameter. The arrangement should prevent particle entrapment and side-of-stem leakage during the delivery of the sample.

Method—Remove the pressurised container from the actuator and remove all labels and markings which may be present on the container with a suitable solvent. Dry the container, replace in its actuator, shake for about 30 seconds and holding it in an inverted position actuate the valve by discharging about 5 sprays to waste. Remove the actuator and wash it thoroughly with *methyl alcohol* and allow it to dry. Clean the valve stem and the valve ferrule by washing with *methyl alcohol* and allow it to dry.

Place about 80 ml of *dehydrated methyl alcohol* in the sampling vessel, shake the pressurised container for about 30 seconds and place it inverted in the vessel over the base plate. Discharge 5 deliveries below the surface of the solvent, actuating the valve at intervals of not less than 15 seconds and discharging the pressurised inhalation through the hole in the centre of the base plate. Repeat the operation until a total of 40 deliveries has been discharged. After every five sprays the container may have to be shaken; where this is done, shaking should be carried out without removing the pressurised container from its inverted position in the vessel. Rinse the valve with small quantities of *dehydrated-methyl alcohol* and dilute the combined solution and washings to 100.0 ml with *dehydrated methyl alcohol*. On 10.0 ml of the resulting solution carry out the **Assay** and calculate the content of Beclomethasone Dipropionate, $C_{28}H_{37}ClO_7$, in μg per actuation of the valve (A). Fit the washed and dried actuator to the pressurised container and actuate the valve 40 times at intervals of not less than 15 seconds. Remove the actuator carefully from the container and wash it with small quantities, each of 5 ml, of *dehydrated methyl alcohol*. Add sufficient *dehydrated methyl alcohol* to produce 25.0 ml. On 20.0 ml of the resulting solution carry out the **Assay** and calculate the content of Beclomethasone Dipropionate, $C_{28}H_{37}ClO_7$, in μg per actuation of the valve (B). Calculate the unit spray content in μg of Beclomethasone Dipropionate, $C_{28}H_{37}ClO_7$, from the expression A-B.

Particle size: Prime the valve by alternately shaking and discharging several times through the actuator and then actuate once on to a clean, dry microscope slide held 5 cm from the end of the actuator, and perpendicular to the direction of the spray. Add 1 ml of *carbon tetrachloride* carefully near the spot where the spray has impinged on the slide and drain after two or three seconds with minimum tilting of the slide. Allow to dry and examine under a microscope, equipped with a calibrated ocular micrometer using 450x magnification. Focus on the particles of 25 fields of view near the centre of the test specimen pattern, and note the size of the great majority of the individual particles; they are not more than 5 μm in diameter. Record the number and size of all individual particles (not agglomerates) more than 10 μm in length measured along the longest axis. Not more than ten such particles are observed and no individual particle exceeds 20 μm in length.

Other requirements: Complies with the requirements stated under Aerosols.

Assay: Remove all labels and any markings on the container with a suitable solvent. Place the container in a plastic bag, cool to at least −20° in a refrigerator and then carefully pierce a small hole on the shoulder of the container. Allow the propellants to evaporate (about 3 hours) and remove the top. Wash the top and valve of the opened can with *dehydrated methyl alcohol*. Transfer the contents of the container and the washing to a 100-ml volumetric flask, dilute to volume with *dehydrated methyl alcohol* and mix. Dilute a suitable volume with *dehydrated methyl alcohol* to produce a solution containing 20 μg of Beclomethasone Dipropionate per ml. To 10.0 ml of the resulting solution add 10 ml of *dehydrated methyl alcohol*, 2.0 ml of *blue tetrazolium solution* and mix; add 2 ml of *tetramethylammonium hydroxide solution* and mix; add 2.0 ml of *tetramethylammonium hydroxide solution (10 per cent)*, mix and allow to stand in the dark for exactly two hours at 37°. Cool to room temperature and add sufficient *dehydrated methyl alcohol* to produce 25.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at about 525 nm against a blank prepared in the same manner using 20 ml of *dehydrated methyl alcohol* instead of the solution of the substance being examined. Calculate the content of Beclomethasone Dipropionate, $C_{28}H_{37}ClO_7$, from the *extinction* obtained by repeating the **Assay** using a solution containing 20 µg of *beclomethasone dipropionate R.S.* per ml and from the declared content of $C_{28}H_{37}ClO_7$ in the *beclomethasone dipropionate R.S.*, Appendix 5.15A.

Storage: Store in small, non-reactive, light-resistant metal aerosol containers with metered-dose valves and provided with oral inhalation actuators. Store in a cool place protected from moisture. Empty containers must also be protected from heat and direct sunlight.

Labelling: The label on the container states (1) the number of metered doses from the container; (2) the amount of active ingredient in the container; (3) the amount of active ingredient delivered per inhalation; (4) that the container should be shaken before use each time; (5) the recommended dose; (6) that it is dangerous to exceed the recommended dose; (7) a warning that the container is pressurised and must be kept away from heat and direct sunlight and must not be punctured, broken or incinerated even when apparently empty; and (8) the warning "keep out of reach of children".

Betamethasone Valerate Ointment

Category: Adrenocortical steroid (topical anti-inflammatory).

Usual strengths: The equivalent of 0.025 per cent and 0.1 per cent w/w of betamethasone

Standards: Betamethasone Valerate Ointment contains Betamethasone Valerate equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of betamethasone, $C_{22}H_{29}FO_5$.

Identification: Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 20 volumes of *chloroform*, 2 volumes of acetone and 1 volume of *ethyl alcohol* as the mobile phase. Apply separately to the plate 10 µl of each of the following solutions: For solution (1) heat a quantity of the ointment equivalent to 1 mg of betamethasone with 10 ml of *methyl alcohol* on a water-bath until it boils, shake vigorously, cool in ice for 30 minutes filter, evaporate the filtrate to dryness in a current of nitrogen with gentle heating and dissolve the residue in 0.5 ml of *chloroform.* For solution (2) use a 0.24 per cent w/v solution of *betamethasone valerate R.S.* in *chloroform.* After removal of the plate allow it to dry in air, heat at 105° for five minutes and spray while hot with *alkaline blue tetrazolium solution.* The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

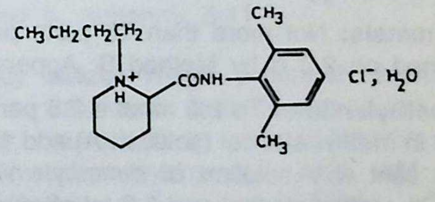
Microbial limits: 1 g meets the requirements of the test for the absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa,* Appendix 4.5.

Assay: Weigh accurately a quantity equivalent to 1.0 mg of Betamethasone and add 30 ml of *aldehyde-free ethyl alcohol.* Heat on a water-bath, mix, cool in ice water and filter into a 100-ml volumetric flask through a plug of absorbent cotton previously washed with *aldehyde-free ethyl alcohol.* Repeat the extraction with three further quantities, each of 20 ml, of *aldehyde-free ethyl alcohol.* Mix the extracts and dilute to volume. Carry out the *assay of steroids,* Appendix 3.3.10, using *betamethasone valerate R.S.* containing about 12.14 µg per ml of the standard.

Storage: Store in well-closed, light-resistant containers. Avoid exposure to excessive heat.

Labelling: The label on the container states the strength in terms of the equivalent amount of betamethasone.

Bupivacaine Hydrochloride



$C_{18}H_{28}N_2O,HCl,H_2O$ Mol.Wt. 342.91

Category: Local anaesthetic.

Dose: By infiltration anaesthesia, the equivalent of 2 mg of anhydrous bupivacaine hydrochloride per kg of body weight.

Description: White, crystalline powder; odourless or almost odourless.

Solubility: Soluble in *water;* freely soluble in *alcohol;*

soluble in *chloroform*, in *acetone* and in *solvent ether*.

Standards: Bupivacaine Hydrochloride is 1-butyl-2-piperidylformo-2′,6′-xylidide hydrochloride monohydrate. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_{18}H_{28}N_2O,HCl$, calculated with reference to the dried substance.

Identification: (A) Dissolve 0.1 g in 5 ml of *water*, add 2 ml of *strong ammonia solution* and filter. Wash the precipitate with *water* and dry at 60° "in vacuo". The *infra-red absorption spectrum* of the residue exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum obtained with *bupivacaine hydrochloride R.S.* treated in a similar manner, Appendix 5.15B.

(B) Dissolve 0.15 g in 10 ml of *water* and add 15 ml of *picric acid solution*. The precipitate, after rapid washing with a small quantity of *water* followed by successive quantities, each of 2 ml, of *methyl alcohol* and *solvent ether* melts at about 194°, Appendix 5.11.

(C) A solution (1 in 20) gives reaction A of *chlorides*, Appendix 3.1.

(D) It melts at about 250°, Appendix 5.11.

pH: Between 4.5 and 6.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Light absorption: Dissolve 40 mg in sufficient *0.01N hydrochloric acid* to produce 100 ml. *Extinction* of a 1-cm layer of the resulting solution at about 263 nm, 0.53 to 0.58 and at about 271 nm, 0.43 to 0.48, Appendix 5.15A.

Heavy metals: Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

2,6-Dimethylaniline: To 2.0 ml of a 2.5 per cent w/v solution in *methyl alcohol* (solution A) add 1.0 ml of a 1.0 per cent w/v solution of *dimethylaminobenzaldehyde* in *methyl alcohol* and 2.0 ml of *glacial acetic acid* and allow to stand for 10 minutes at room temperature. The yellow colour produced is not more intense than that obtained by using 2.0 ml of a solution in *methyl alcohol* containing 2.5 µg of *2,6-dimethylaniline* per ml in place of solution A.

Related substances: Carry out the method for *thin-layer chromatogrphy*, Appendix 5.4.3, using *silica gel G* as the coating substance and *alcohol* as the mobile phase. Apply separately to the plate 2 µl of each of the two solutions in *methyl alcohol* containing (1) 5.0 per cent w/v and (2) 0.050 per cent w/v of the substance being examined. After removal of the plate allow it to dry in air until the odour of the solvent is no longer detectable, and spray with *dilute potassium iodobismuthate solution*. Any spot in the chromatogram obtained with solution (1) other than the principal spot is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash: Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying: Not less than 4.5 per cent and not more than 6.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8

Assay: Weigh accurately about 0.6 g, dissolve in 20 ml of *glacial acetic acid* and add 10 ml of *mercuric acetate solution*. Add a few drops of *crystal violet solution* and titrate with *0.1N perchloric acid* to a bluish-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03249g of $C_{18}H_{28}N_2O,HCl$.

Storage: Store in well-closed containers.

Bupivacaine Injection

Bupivacaine Hydrochloride Injection

Category: Local anaesthetic.

Dose: By infiltration anaesthesia, the equivalent of 2 mg of anhydrous bupivacaine hydrocloride per kg of body weight.

Usual strengths: The equivalent of 25, 50 and 75 mg of anhydrous bupivacaine hydrochloride in 10 ml.

Standards: Bupivacaine Injection is a sterile solution of Bupivacaine Hydrochloride in Water for Injection. It contains not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of anhydrous bupivacaine hydrochloride, $C_{18}H_{28}N_2O,HCl$.

Description: Colourless or almost colourless solution.

Identification: (A) Dilute a suitable volume with sufficient *0.0IN hydrochloric acid* to produce a solution containing the equivalent of 0.05 per cent w/v of anhydrous bupivacaine hydrochloride. The light absorption, in the range 230 to 350 nm, exhibits two maxima, at about 263 nm and 271 nm. *Extinction* at 263 nm is about 0.70 and at 271 nm is about 0.57, Appendix 5.15A.

(B) A volume containing the equivalent of 50 mg of anhydrous bupivacaine hydrochloride complies with **Identification** test (B) described under Bupivacaine Hydrochloride.

(C) To a volume containing the equivalent of 50 mg of anhydrous bupivacaine hydrochloride, add 2 ml of a 10 per cent w/v solution of *disodium hydrogen phosphate* and sufficient *iodine solution* to produce a distinct brown colour. Remove the excess iodine by adding *0.1N sodium thiosulphate.* No pink colour is produced.

pH: Between 4.0 and 6.5, Appendix 5.10.

2,6-Dimethylaniline: To a volume containing the equivalent of 25 mg of anhydrous bupivacaine hydrochloride add *water,* if necessary, to produce 10 ml and sufficient *2N sodium hydroxide* to make the solution just alkaline. Extract with three quantities, each of 5 ml, of *chloroform.* Dry the combined chloroform extracts over *anhydrous sodium sulphate,* filter, wash the filter with 5 ml of *chloroform* and evaporate the filtrate to dryness using a rotary evaporator. Dissolve the residue in 2.0 ml of *methyl alcohol* (solution A). Complete the test described under Bupivacaine Hydrochloride, beginning at the words, "add 1.0 ml of a 1.0 per cent w/v solution of *dimethylaminobenzaldehyde...*"

Related substances: Carry out the test for **Related substances** described under Bupivacaine Hydrochloride. For solution (1) evaporate almost to dryness a volume equivalent to 0.1 g of anhydrous bupivacaine hydrochloride using a rotary evaporator, dilute the residue with sufficient *methyl alcohol* to produce 2 ml, mix well, centrifuge and use the supernatant liquid. For solution (2) dilute 1 volume of solution (1) to 100 volumes with *methyl alcohol.*

Other requirements: Complies with the requirements stated under Injections.

Assay: To a volume equivalent to 75 mg of anhydrous bupivacaine hydrocholride add 5 ml of *water* and 2 ml of *N sodium hydroxide* and extract with three quantities, each of 15 ml, of *chloroform.* Combine the chloroform extracts and wash with two quantities, each of 5 ml, of *water, wash the* aqueous solution with 5 ml of *chloroform* and evaporate the combined chloroform extracts to dryness on a water-bath. Add two successive quantities, each of 5 ml, of *acetone* and evaporate; dissolve the residue in 50 ml of *glacial acetic acid,* add 10 ml of *mercuric acetate solution* and a few drops of *crystal violet solution.* Titrate with *0.1N perchloric acid* to a bluish-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03249 g of $C_{18}H_{28}N_2O$,HCl.

Storage: Store in single dose or multiple-dose containers, preferably of Type I glass.

Labelling: The label on the container states the strength in terms of the equivalent amount of anhydrous bupivacaine hydrochloride in a suitable dose-volume.

Hydrogenated Castor Oil

Castor Wax, Opalwax

Category: Pharmaceutical aid (stiffening agent, coating material.)

Description: White or slightly yellow flakes or drops. It may have a hard, waxy consistency.

Solubility: Insoluble in *water;* soluble in *acetone,* in *chloroform* and in *carbon tetrachloride.*

Standards: Hydrogenated Castor Oil is refined, bleached, hydrogented and deodorised castor oil. It consists mainly of the triglyceride of hydroxystearic acid.

Melting range: Between 85° and 88°, determined by Method II, Appendix 5.11.

Free fatty acids: Weigh accurately about 20 g, melt on a water-bath, add 75 ml of hot *alcohol,* previously neutralised to *phenolphthalein solution* with *0.1N sodium hydroxide,* swirl, add 1 ml of *phenolphthalein solution* and titrate with *0.1N sodium hydroxide,* swirling vigorously until the solution remains faintly pink after being shaken for 60 seconds; not more than 11.0 ml *0.1N sodium hydroxide* is required.

Hydroxyl value: Between 154 and 162, Appendix 3.3.17.

Iodine value: Not more than 5.0, Appendix 3.3.18.

Saponification value: Between 176 and 182, Appendix 3.3.20.

Heavy metals: Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Storage. Store in tightly-closed containers in a cool place.

Labelling: The label on the container states "Avoid exposure to excessive heat".

Caramel

Burnt Sugar

Category: Pharmaceutical aid (colouring agent).

Description: Thick, free-flowing, dark brown liquid: odour, slight and characteristic; taste, bland.

Solubility: Miscible with *water,* with dilute alcohols (upto about 60 per cent v/v) with dilute mineral acids, and with *sodium hydroxide* solutions; immiscible with *chloroform* and with *solvent ether.* It is precipitated by strong alcohols (more than 60 per cent v/v).

Standards: Caramel is a concentrated solution of the product obtained by heating Sucrose or Dextrose until the sweet taste is destroyed.

Identification: To 20 ml of a 5 per cent w/v solution add 0.5 ml of *phosphoric acid;* no precipitate is produced.

Wt. per ml: Not less than 1.30 g, Appendix 5.19.

pH: Between 3.0 and 5.5 determined in a 10 per cent w/v solution, Appendix 5.10.

Acid-stability: Dilute 50 ml of a 1 per cent w/v solution to 250 ml with *water,* add 5 ml of *hydrochloric acid* and heat gently to boiling under reflux. Allow to cool and set aside for 24 hours; solution remains clear. Repeat the test on the same test solution but boil for 30 minutes. The solution remains clear for 24 hours.

Arsenic: Not more than 5 parts per million, Appendix 3.2.1.

Heavy metals: Not more than 10 parts per million, determined on 2.0 g by method B, Appendix 3.2.4.

Iron: Evaporate 0.40 g to dryness, add 0.2 ml of *nitric acid,* ignite and dissolve the residue in 1 ml of *dilute nitric acid:* the solution complies with the *limit test for iron,* Appendix 3.2.5.

Microbial limits: 1 g meets the requirements of the tests for the absence of *E. coli* and *salmonellae,* Appendix 4.5.

Sulphated ash: Not more than 2.0 per cent, determined on 1.0 g, Appendix 3.2.7.

Storage: Store in tightly-closed containers.

Carnauba Wax

Category: Pharmaceutical aid (tablet coating agent).

Description: Pale yellow to light brown coarse powder or flakes or lumps of hard brittle wax; odour, characteristic and free from rancidity.

Solubility: Practically insoluble in *water,* slightly soluble in boiling *alcohol,* soluble in warm *chloroform* and in warm *toluene.*

Standards: Carnauba Wax is the wax obtained from the leaves of *Copernicia cerifera* Mart, after purification by the removal of foreign matter.

Melting range: Between 78° and 85°, Appendix 5.11.

Acid Value: Not more than 12.0, Appendix 3.3.15.

Iodine value: Between 7 and 14, Appendix 3.3.18.

Saponification value: Between 75 and 95, Appendix 3.3.20.

Heavy metals: Not more than 40 parts per million, determined on 0.5 g by Method B, Appendix 3.2.4.

Sulphated ash: Not more than 0.25 per cent, Appendix 3.2.7.

Storage: Store in tightly-closed containers.

Cetyl Alcohol

Palmityl Alcohol; n-Hexadecyl Alcohol; 1-Hexadecanol

Category: Pharmaceutical aid (stiffening, emulsifying and tablet coating agent).

Description: White, unctuous mass, powder, flakes or granules; odour, slight.

Solubility: Practically insoluble in *water:* freely soluble in *solvent ether;* sparingly soluble in *alcohol.* When melted it is miscible with *liquid paraffin,* with animal and vegetable oils and with melted *wool fat.*

Standards: Cetyl Alcohol is a mixture of solid alcohols consisting mainly of 1-hexadecanol, $C_{16}H_{34}O$.

Melting Range: Between 46° and 52°, Appendix 5.11.

Hydroxyl value: Between 218 and 238, Appendix 3.3.17.

Acid value: Not more than 1.0, Appendix 3.3.15.

Iodine value: Not more than 2.0, determined by Method B on 2.0 g dissolved in 25 ml of *chloroform*, Appendix 3.3.18.

Saponification value: Not more than 2.0, Appendix 3.3.20.

Storage: Store in well-closed containers.

Chlorhexidine Gluconate Solution

Category: Antiseptic.

Description: Almost colourless to pale straw-coloured, clear or slightly opalescent liquid; almost odourless.

Solubility: Miscible with *water*, with upto 5 parts of *alcohol* and upto 3 parts of *acetone*.

Standards: Chlorhexidine Gluconate Solution is an aqueous solution of 1,1-hexamethylenebis[5-(4-chlorophenyl)biguanide] digluconate. It contains not less than 19.0 per cent w/v and not more than 21.0 per cent w/v of $C_{22}H_{30}Cl_2N_{10},2C_6H_{12}O_7$.

Identification: (A) To 1 ml add 40 ml of *water*, cool to about 10°, add *sodium hydroxide solution* dropwise with stirring until the solution is slightly alkaline to *titan yellow paper* and add 1 ml in excess. Filter, wash the precipitate with water until the washings are no longer alkaline to *titan yellow paper*, recrystallise from *alcohol (70 per cent)* and dry at 105°. The *infra-red absorption spectrum* of the residue exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, these in the spectrum obtained with *chlorhexidine hydrochloride R.S.* treated in a similar manner, Appendix 5.15B.

(B) To 0.5 ml add 10 ml of *water* and 0.5 ml of *copper sulphate solution;* a white precipitate is produced which on boiling flocculates and changes to a pale purple colour.

(C) To 0.05 ml add 5 ml of a warm 1 per cent w/v solution of *cetrimide*, 1 ml of *sodium hydroxide solution* and 1 ml of *bromine water;* a deep red colour is produced.

pH: Between 5.5 and 7.0, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Wt. per ml: Between 1.06 and 1.07 g, determined at 20° in a 5 per cent w/v solution, Appendix 5.19.

Related substances: Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a plate 0.5 mm thick prepared by using a slurry consisting of 8 g of *silica gel GF 254* and 16 ml of *water* containing 1 g of *sodium formate.* Use a mixture of 50 volumes of *chloroform*, 50 volumes of *alcohol* and 7 volumes of *formic acid* as the mobile phase. Apply to the plate in the form of a band 4 cm wide, 20 µl of a solution obtained by diluting 5 ml of the substance being examined, to 100 ml with *1.5N acetic acid* (solution 1). After removal of the plate, allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. Mark the area around each group of bands above and below the principal band, transfer quantitatively the enclosed areas of silica gel to a glass-stoppered tube, add 5.0 ml of *methyl alcohol*, shake for fifteen minutes, centrifuge and measure the *extinction* of a 1-cm layer of the clear, supernatant liquid at about 256 nm, Appendix 5.15A, using as the blank a solution prepared by heating in a similar manner equivalent-sized areas of silica gel removed from the coating adjacent to the areas previously removed. The *extinction* is not greater than the *extinction* obtained from solution (2) prepared by diluting 2 ml of the substance being examined with sufficient *1.5N acetic acid* to produce 10 ml and diluting 0.2 ml of this solution to 50 ml with *methyl alcohol.*

4-Chloroaniline: Dilute 2.0 ml to 100.0 ml with *water.* To 10.0 ml of this solution in a 50-ml volumetric flask add 20 ml of *water* and, with continuous mixing, 5 ml of *N hydrochloric acid*, 1 ml of a 0.1 per cent w/v solution of *sodium nitrite* and 2 ml of a 5 per cent w/v solution of *ammonium sulphamate.* Add 5 ml of a 0.1 per cent w/v solution of *N-(1-naphthyl)ethylenediamine hydrochloride*, 1 ml of *alcohol* and dilute to volume with *water.* Keep aside for thirty minutes. Any colour produced is not deeper than that produced by treating in the same manner 10.0 ml of a 0.0010 per cent w/v solution of *4-chloroaniline* in *water* slightly acidified with *hydrochloric acid*, and beginning at the words "add 20 ml of *water........*".

Sulphated ash: Not more than 0.2 per cent w/v, Appendix 3.2.7.

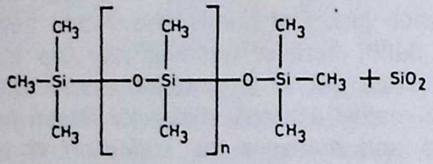
Assay: Weigh accurately about 5 g and evaporate to a low bulk. Dissolve in 50 ml of *glacial acetic acid.*

Titrate with *0.1N perchloric acid,* determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02244 g of $C_{22}H_{30}Cl_2N_{10},2C_6H_{12}O_7$. From the wt. per ml calculate the percentage of $C_{22}H_{30}Cl_2N_{10},2C_6H_{12}O_7$ weight in volume.

Storage: Store in well-closed, light-resistant containers in a cool place.

Activated Dimethicone

Activated Polydimethylsiloxane; Simethicone



$(CH_3)_3Si[OSi(CH_3)_2]CH_3+SiO_2$

Category: Defoaming agent.

Dose: 40 to 100 mg, four times daily.

Description: Translucent, grey, viscous liquid; almost odourless; tasteless.

Solubility: Insoluble in *water* and in *alcohol;* the liquid phase is soluble in *chloroform,* in *solvent ether* and in *benzene,* but silicon dioxide remains as a residue in the solvent.

Standards: Activated Dimethicone is a mixture of fully methylated linear siloxane polymers containing repeating $-(CH_3)_2SiO-$ units stabilised with trimethylsiloxy, $(CH_3)_3SiO-$, end-blocking units and finely divided silicon dioxide. It contains not less than 90.0 per cent and not more than 99.0 per cent of polydimethylsiloxane $[-(CH_3)_2SiO-]_n$, and not less than 4.0 per cent and not more than 7.0 per cent of silicon dioxide.

Identification: To 50 mg add 25 ml of *carbon tetrachloride* and swirl to disperse. Add 50 ml of *dilute hydrochloric acid* and shake for five minutes. Transfer to a separator and remove about 5 ml of the lower layer to a stoppered-tube containing 0.5 g of *anhydrous sodium sulphate.* Shake vigorously and centrifuge the mixture until a clear supernatant liquid is obtained. The *infra-red absorption spectrum* of the resulting solution exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of a solution of *polydimethylsiloxane R.S.,* Appendix 5.15B.

Heavy metals: Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Defoaming activity: Prepare a test solution by transferring 0.2 g to a 100-ml bottle, add 50 ml of *t-butyl alcohol* and shake vigorously, warming, if necessary, to effect solution. Add dropwise, 0.5 ml of this solution to a clean, unused, cylindrical 250-ml glass jar, fitted with a 50-mm cap, containing 100 ml of a 1.0 per cent w/v solution of *octoxynol.* Cap the jar and clamp it in an upright position in a wrist-action shaker capable of moving the jar through a radius of 13.3 ± 0.4 cm (measured from centre of shaft to centre of jar) and an arc of 10 degrees at a frequency of 300 ± 30 strokes per minute. Shake for 10 seconds and record the time required in seconds for the foam to collapse. The time for foam collapse is determined at the instant the first portion of foam-free liquid surface appears, measured from the end of the shaking period. The defoaming activity time is not more than 15 seconds.

Silicon dioxide content: Mix thoroughly and transfer about 1 g, accurately weighed, to a tared, fine-porosity, sintered-glass (G 4 grade is suitable) filtering crucible. Pass through the filter with suction 200 ml of *carbon tetrachloride,* added with stirring in small portions, followed by similar washing of the material in the filter with 200 ml of *n-hexane,* and discard the filtrates. Place the filtering crucible in a muffle furnace at room temperature, purge the furnace chamber with nitrogen, and, while maintaining the flow of nitrogen, raise the furnace temperature to 550°. Heat at 550 ± 25° for two hours, maintaining a steady flow of nitrogen. Cool the filtering crucible with its contents in a desiccator, weigh and calculate the content of silicon dioxide, SiO_2, in the sample taken.

Assay: Weigh accurately about 50 mg, transfer to a narrow-mouthed glass bottle and add 25 ml of *carbon tetrachloride.* Swirl to disperse, add 50 ml of *dilute hydrochloric acid,* close the bottle securely with a cap having an inert liner, and shake for exactly five minutes. Transfer the mixture to a 125-ml separator, and remove about 5 ml of the lower layer to a stoppered test-tube containing 0.5 g of *anhydrous sodium sulphate.* Close the test-tube, agitate vigorously, and centrifuge the mixture until a clear supernatant liquid is obtained. Prepare a blank by mixing 10 ml of *carbon tetrachloride* with 0.5 g of *anhydrous sodium sulphate* and centrifuging to obtain a clear supernatant' liquid. Determine the *extinction* of a 0.5-mm layer of the solution at the maximum at about 7.9 µm with a suitable infra-red spectrophotometer, Appendix 5.15B, using the blank to set the instrument. Calculate the content of $[-(CH_3)_2SiO-]_n$ from the *extinction* obtained by repeating the assay on a 0.2 per cent w/v solution of *polydimethylsiloxane R.S.* in place of the substance being examined and from the declared content of $[-(CH_3)_2SiO-]_n$ in the *polydimethylsiloxane R.S.*

Storage: Store in tightly-closed containers.

Ethosuximide Syrup

Category: Anticonvulsant.

Dose: Ethosuximide. For children: 50 to 125 mg twice daily, increasing to 250 mg, three or four times daily, as necessary. For adults: 500 mg daily, in divided doses, increasing to 2 g daily, as necessary.

Usual strength: 250 mg in 5 ml.

Standards: Ethosuximide Syrup contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Ethosuximide, $C_7H_{11}NO_2$.

Identification: (A) Extract a quantity equivalent to 500 mg of Ethosuximide with two quantities, each of 30 ml, of *chloroform,* filter the combined extracts through a plug of cotton, and evaporate the filtrate to dryness. Heat 100 mg of the residue with 0.2 g of *resorcinol* and 0.1 ml of *sulphuric acid* at 140° for five minutes, add 5 ml of *water,* make alkaline with *sodium hydroxide solution* and pour a few drops into a large volume of *water;* a bright green fluorescence is obtained.

(B) In the **Assay** the chromatogram obtained with solution (2) shows a peak having the same retention time as the peak due to *ethosuximide R.S.* in the chromatogram obtained with solution (1).

Assay: Carry out the method for *gas-liquid chromatography,* Appendix 5.4.1, using the following solutions. For solution (1) mix 25 ml of a 0.2 per cent w/v solution of *ethosuximide R.S.* in *chloroform* with 2 ml of a 3.0 per cent w/v solution of *dimethyl phthalate* (internal standard) in *chloroform;* solution (2) is prepared in a similar manner to solution (3) but omitting the internal standard; for solution (3) add 10 ml of *water* and 2 g of *sodium bicarbonate* to a quantity of the syrup equivalent to 250 mg of Ethosuximide, extract with five quantities, each of 25 ml of *chloroform,* washing each extract with the same 10 ml of *water,* shake with 10 g of *anhydrous sodium sulphate,* and filter; add 10 ml of a 3.0 per cent w/v solution of *dimethyl phthalate* (internal standard) in *chloroform,* evaporate the combined chloroform solutions to dryness under reduced pressure at a temperature not exceeding 40°, and dissolve the residue in 5 ml of *chloroform.* Carry out the chromatographic procedure using (a) a glass column 1.5 m long and 4 mm in internal diameter packed with 3 per cent w/w of cyanopropylmethyl phenyl methyl silicone fluid (OV-225 is suitable) coated on acid-washed silanised diatomaceous support (80 to 100 mesh) (Gas Chrom Q is suitable) maintained at 165°, and an inlet port temperature of 240°; (b) nitrogen as the carrier gas; and (c) a flame ionisation detector. Calculate the content of $C_7H_{11}NO_2$ from the declared content of $C_7H_{11}NO_2$ in the *ethosuximide R.S.*

Storage: Store in well-closed containers in a cool place.

Ethylcellulose

Cellulose ethyl ether

Category: Pharmaceutical aid (tablet excipient)

Description: White to light tan powder; almost odourless.

Solubility: Insoluble in *water,* in *glycerin* and in *propylene glycol.* Ethylcellulose containing more than 46.5 per cent of ethoxy groups is freely soluble in *alcohol,* in *methyl alcohol,* in *chloroform* and in *ethyl acetate.*

Standards: Ethylcellulose is an ethyl ether of cellulose. It contains not less than 44.0 per cent and not more than 51.0 per cent of ethoxy $(-OC_2H_5)$ groups, calculated with reference to the dried substance.

Identification: (A) Dissolve 15 mg of the dried sample in 10 ml of dried *methylene chloride.* Grind 0.5 ml of this solution to dryness with 300 mg of *potassium bromide.* The *infra-red absorption spectrum* of the residue exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *ethylcellulose R.S.,* Appendix 5.15B.

pH: Between 5.5 and 8.0, Appendix 5.10, determined in a solution prepared in the following manner. Stir

1.0 g with 50 ml of *carbon dioxide-free water* previously heated to 90°, then cool and dilute with sufficient *carbon dioxide-free water* to produce 100 ml.

Apparent viscosity: Not less than 90.0 per cent and not more than 110.0 per cent of that stated on the label for viscosity types of 10 centipoises or more; not less than 80.0 per cent and not more than 120.0 per cent of that stated on the label for viscosity types of 6 to 10 centipoises; and not less than 75.0 per cent and not more than 140.0 per cent of that stated on the label for viscosity types of 6 centipoises or less; determined on a 5.0 per cent w/w solution by the following method. Weigh accurately about 5.0 g, calculated with reference to the dried substance, and dissolve in 95.0 ± 0.05 g of a mixture of 80 parts of *toluene* and 20 parts of *alcohol*. For ethylcellulose containing less than 46.5 per cent ethoxy groups use a mixture of 60 parts of *toluene* and 40 parts of *alcohol* by weight. Determine the *viscosity* at 25° by Method A, Appendix 5.18.

Arsenic: Not more than 3 parts per million, Appendix 3.2.1.

Heavy metals: Not more than 40 parts per million, determined on 0.5 g by Method B, Appendix 3.2.4.

Sulphated ash: Not more than 0.5 per cent, Appendix 3.2.7.

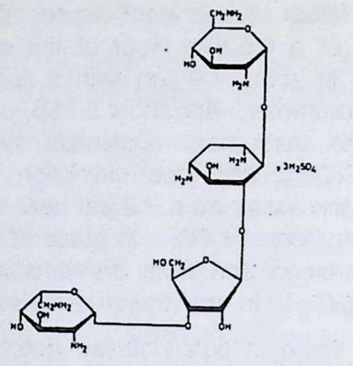
Loss on drying: Not more than 3.0 per cent, determined on 1.0 g by drying in an oven at 105° for 2 hours, Appendix 5.8.

Assay: Weigh accurately about 50 mg in an empty, tared Hard Gelatin Capsule Shell and place the capsule and contents in the boiling flask of the apparatus in the method for the *determination of methoxyl*, Appendix 3.3.3. Proceed as directed in the appendix. Each ml of *0.1N sodium thiosulphate* is equivalent to 0.0007510 g of ethoxy ($-OC_2H_5$) groups.

Storage: Store in well-closed containers.

Labelling: The label on the container states the apparent viscosity in centipoises of a 2.0 per cent w/v solution and its ethoxy content.

Framycetin Sulphate



$C_{23}H_{46}N_6O_{13},3H_2SO_4$ Mol. Wt. 908.87

Category: Antibacterial (topical).

Description: White or yellowish-white powder; odourless or almost odourless; hygroscopic.

Solubility: Freely soluble in *water;* very slightly soluble in *alcohol;* practically insoluble in *acetone,* in *chloroform* and in *solvent ether.*

Standards: Framycetin Sulphate is the sulphate of 2-deoxy-4-*O*-(2,6-diamino-2,6-dideoxy-α-D-glucopyranosyl)-5-*O*-[3-*O*-(2,6-diamino-2,6-dideoxy-β-L-idopyranosyl)-β-D-ribofuranosyl] streptamine (neomycin B), a substance produced by the growth of selected strains of *Streptomyces fradiae* or *Streptomyces decaris* or by any other means. It contains an amount of framycetin sulphate equivalent to not less than 630 µg of neomycin B per mg, calculated with reference to the dried substance.

Identification: (A) Carry out the method for *thin-layer chromatography,* Appendix 5.4.3, using a plate prepared immediately before use as described in the test for **Neamine** and a 10 per cent w/v solution of *potassium dihydrogen phosphate* as the mobile phase. Apply separately to the plate 10 µl of each of three solutions containing (1) 0.1 per cent w/v of the substance being examined, (2) 0.1 per cent w/v of *framycetin sulphate R.S.* and (3) 0.1 per cent w/v each of *framycetin sulphate R.S., kanamycin sulphate R.S.* and *streptomycin sulphate R.S.* Allow the solvent to rise 15 cm above the line of application. After removal of the plate, allow it to dry in air and spray with a mixture of equal volumes of a 46 per cent w/v solution of *sulphuric acid* and of a 0.2 per cent w/v solution of *1,3-naphthalenediol* in *alcohol* and heat at 150° for about ten minutes. The principal spot in the chromatagram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). The test is valid only when the chromatogram obtained with solution (3) shows three clearly separated principal spots.

(B) Dissolve 10 mg in 5 ml of *water*, add 0.1 ml of *pyridine* and 2 ml of a 0.1 per cent w/v solution of *ninhydrin* and heat in a water-bath at 65° to 70° for ten minutes. An intense violet colour is produced.

(C) A solution (1 in 20) gives the reactions of *sulphates*, Appendix 3.1.

pH: Between 6.0 and 7.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Specific optical rotation: Between +52.0° and +55.5°, determined at 20° in a 10 per cent w/v solution, Appendix 5.12.

Neamine: Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a 10 per cent w/v solution of *potassium dihydrogen phosphate* as the mobile phase and a plate prepared in the following manner. Mix 0.3 g of *carbomer* with 240 ml of *water*, allow to stand for one hour with moderate shaking, adjust to pH 7 by the gradual addition of *2N sodium hydroxide* and add 30 g of *silica gel H*. Spread a uniform layer of the suspension 0.75 mm thick, heat at 110° for one hour, allow to cool and use the plate immediately. Apply separately to the plate 10 µl of each of two solutions containing (1) 0.50 per cent w/v of the substance being examined; and (2) 0.005 per cent w/v of *neamine R.S.* Allow the solvent to rise 15 cm above the line of application. After removal of the plate, allow it to dry in a current of warm air, spray with *ninhydrin-stannous chloride solution*, and heat at 110° for fifteen minutes. Any spot corresponding to neamine in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (2).

Neomycin C: *Apparatus*—A chromatographic column 6 mm in diameter and 40 cm long, maintained at a constant uniform temperature (±1°) between 10° and 20° and provided with suitable means of passing eluent down the column at a constant rate. The column is mounted over a fraction collector.

Reagents—(a) *Water*, freshly boiled and prepared by double distillation in a glass-still, cooled, and protected from atmospheric carbon dioxide.

(b) An anion-exchange resin such as Bio-Rad AG1X2.

Method—Introduce into the column to within 1 cm of the top successive portions of a suspension of the resin in *water* and wash the column for 90 minutes. Apply to the surface of the resin 0.1 ml of a 1 per cent w/v solution of the substance being examined in *water* and use *water* adjusted to pH 7.5 with *0.01N sodium hydroxide* as the mobile phase. Adjust the flow rate of the mobile phase to 1 ml per minute. Collect the eluate in 1-ml fractions. Add 2 ml of *ninhydrin reagent* to each fraction, heat in a water-bath for fifteen minutes, allow to cool and measure the *extinction* at about 570 nm, Appendix 5.15A, using 1 ml of *water* treated in the same manner as the blank. If the *extinction* is more than 0.6, dilute the contents of the tube by the addition of 6 ml of a mixture of equal volumes of *alcohol* and *water* and repeat the measurement. Plot a graph from the results obtained, correcting the extinctions for dilution, if necessary, and determine the areas of the peaks corresponding to neomycin B and neomycin C (Neamine is eluted first from the column as a single peak or as a partly-resolved double peak, followed by neomycin C and then neomycin B). The area of the peak corresponding to neomycin C is less than 3.0 per cent of the sum of the areas of the peaks corresponding to neomycin B and neomycin C. The test is not valid unless the *resolution factor* between the peaks corresponding to neomycin B and neomycin C is greater than 1.4. Appendix 5.4.1.

Sulphate: Between 27.0 per cent and 31.0 per cent of SO_4, calculated with reference to the dried substance and determined by the following method. Weigh accurately about 0.25 g, dissolve in 100 ml of *water*, adjust the pH to 11 with *strong ammonia solution* and add 10.0 ml of *0.1N barium chloride.* Titrate with *0.1N disodium ethylenediaminetetraacetate*, using 0.5 mg of *metalphthalein* as indicator; add 50 ml of *alcohol* when the colour of the solution begins to change and continue the titration until the violet-blue colour disappears. Each ml of *0.1N barium chloride* is equivalent to 0.009606 g of SO_4.

Sulphated ash: Not more than 1.0 per cent, determined on 1.0 g, Appendix 3.2.7.

Loss on drying: Not more than 8.0 per cent, determined on 1.0 g by drying 'in vacuo at 60°' for 3 hours, Appendix 5.8.

Assay: Carry out the *microbiological assay of antibiotics*, Method A, Appendix 4.1, and express the results in µg of neomycin B per mg.

Storage: Store in tightly-closed, light-resistant containers in a cool place.

Labelling: The label on the container states (1) the strength in terms of µg of neomycin B per mg; (2) the date after which the contents are not intended to be used; (3) the storage conditions.

Furazolidone Tablets

Category: Antiprotozoal and antibacterial.

Dose: Furazolidone, 400 mg daily, in divided doses.

Usual strengths: 100 mg; 200 mg.

Standards: Furazolidone Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_8H_7N_3O_5$.

Identification: Add a quantity of the powdered tablets equivalent to 50 mg of Furazolidone to 10 ml of a freshly prepared mixture of 9 volumes of *dimethylformamide* and 1 volume of *1N alcoholic potassium hydroxide.* The solution turns purple, immediately changes to deep blue and upon standing for about 10 mintues again turns purple.

Other requirements: Comply with the requirements stated under Tablets.

Assay: Protect the solution from light throughout the assay. Weigh and finely powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.08 g of Furazolidone into a 200-ml volumetric flask. Add about 100 ml of *dimethylformamide,* warm to about 50° and shake well to dissolve the furazolidone. Cool, dilute with *dimethylformamide* to volume, mix and centrifuge a portion of the mixture. Dilute 5.0 ml of the clear solution so obtained to 250 ml with *water* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 367 nm, Appendix 5.15A. Calculate the content of $C_8H_7N_3O_5$, taking 750 as the value of E (1 per cent, 1-cm) at the maximum at about 367 nm.

Storage: Store in well-closed, light-resistant containers.

Hard Gelatin Capsule Shells

Category: Pharmaceutical aid.

Description: Gelatin cases (shells) consisting of two cylindrical, telescoping pieces (cap and body), one end of which is rounded and closed and the other, open. Shapes other than cylindrical can also be formed as per requirements. The two pieces are uncoloured or coloured; if coloured, of identical or different colours; transparent or opaque, partially or completely and printed or unprinted or bear other surface markings. The cap overlaps the body and maintains a tight friction closure. The closure may be strengthened by suitable means.

The shells are of various sizes, usually designated by different numbers, 5 being the smallest and 000 the biggest. Shells of sizes 0 to 4 are commonly used. Shells of special sizes are also available. The shells are smooth and uniform in size, shape and colour.

Standards: Hard Gelatin Capsule Shells are soluble containers for incorporation of drugs, usually in the form of powders, pellets or granules, and are commonly intended for oral administration. The shells are acted upon by digestive fluids and the filled contents are released. They are composed of gelatin, water and additives such as plasticizers, humectants, surfactants, dispersing agents, flavouring agents, antimicrobial agents, sweetening agents, opacifying agents and one or more colouring agents permitted under the Drugs & Cosmetics Rules, 1945. Ingredients other than colouring agents and opacifying agents comply with the standards of this pharmacopoeia.

NOTE—In order to ensure that the quality of the shells is not affected by temperature and humidity, the capsule shells should be conditioned, specially for tests on ***dimensions, brittleness*** *and* ***uniformity of weight,*** *at a temperature of 25 ± 2° and a relative humidity of 50 ± 10 per cent for not less than 12 hours.* (As sizes 0 to 4 are commonly used, detailed requirements in respect of dimensions and uniformity of weight are included for these sizes only in this monograph. Requirements for other sizes may be decided upon mutually between the manufacturer of the Hard Gelatin Capsule Shells and the user).

Identification: Boil one capsule shell with 20 ml of *water,* allow to cool and centrifuge. To 5 ml of the supernatant liquid add 1 ml of *picric acid solution* and to another 5 ml add 1 ml of *tannic acid solution;* a precipitate is produced in each case.

Dimensions: Take 20 capsule shells, meeting with requirements of the **Loss on drying** test, and measure the outer diameter, length of cap and body and joined length of empty shells with a vernier capable of reading upto 0.01 mm. Measure the single and double wall thickness of the cap, 1 mm from the edge, and of the body, 4 mm from the cut edge, with a micrometer graduated in intervals of 0.001 mm. The average values should lie within the limits specified for various sizes in tables 1 to 4.

TABLE 1

Outside diameter

Size	Cap (mm)	Body (mm)
0	7.57 — 7.69	7.26 — 7.38
1	6.85 6.97	6.56 — 6.68
2	6.28 — 6.40	6.01 — 6.13
3	5.75 — 5.87	5.50 — 5.62
4	5.25 — 5.37	5.00 — 5.12

TABLE 2

Length

Size	Cap (mm)	Body (mm)
0	10.82 — 11.54	18.36 — 19.08
1	9.65 — 10.37	16.36 — 17.08
2	8.81 — 9.53	14.98 — 15.70
3	7.87 — 8.59	13.12 — 13.84
4	7.11 — 7.83	11.98 12.70

TABLE 3

Joined length of empty shells

Size	Empty Joined Length (mm)
0	22.67 — 24.17
1	20.34 — 21.84
2	18.77 — 20.27
3	16.88 — 18.18
4	15.30 — 16.80

TABLE 4

Wall thickness

Size	Single Wall Thickness		Double Wall Thickness	
	Cap (mm)	Body (mm)	Cap (mm)	Body (mm)
0	0.095 — 0.120	0.092 — 0.117	0.203 — 0.223	0.193 — 0.213
1	0.092 — 0.117	0.089 — 0.114	0.198 — 0.218	0.191 — 0.211
2	0.089 — 0.114	0.086 — 0.111	0.196 — 0.216	0.189 — 0.209
3	0.086 — 0.111	0.083 — 0.108	0.186 — 0.206	0.181 — 0.201
4	0.083 — 0.108	0.080 — 0.105	0.183 — 0.203	0.180 — 0.200

Brittleness: Take 100 capsule shells devoid of long, short, broken or separated ones. Place each shell on a smooth hard surface. Using a brass rod of 150 mm length and 25 mm diameter and weighing approximately 0.5 kg, press the entire length of the shell until the sides meet. Repeat with another 99 shells. Not more than two shells crack, chip or break. If more than two but less than six shells fail to comply with the test, repeat the test with another 100 shells taken at random. The sample being examined complies if not more than six out of 200 shells fail to comply with the test.

Odour: Keep 100 capsule shells in a well-closed bottle for 24 hours at a temperature between 30° and 40°; the shells do not develop any foreign odour.

Uniformity of weight: Weigh 20 capsule shells and determine the average weight. Not more than two of the individual weights deviate from the average by more than the deviation shown in Table 5 and none deviates by more than twice that deviation.

TABLE 5

Size	Average weight (mg)	Deviation (± mg)
0	100	10.0
1	80	8.0
2	65	6.5
3	50	5.0
4	40	4.0

Disintegration: The capsule shells comply with the *disintegration test for capsules*, using the discs, Appendix 5.6.2. The capsules disintegrate within 15 minutes.

Microbial limits: The total microbial count does not exceed 1000 per g of the capsule shells. 1 g meets the requirements of the tests for the absence of *E. coli* and *salmonellae*, Appendix 4.5.

Loss on drying: Between 12.5 per cent and 16.0 per cent, determined on capsule shells weighing 1.0 g by drying in an oven at 105° for 18 hours, Appendix 5.8.

Storage: Store in well-closed containers in a cool place with relative humidity between 40 per cent and 60 per cent.

Labelling: The label on the container states (1) the size of the capsule shells; (2) that only permitted colours, if any, have been used; (3) the storage conditions.

Hydrocortisone Sodium Succinate Injection

Cortisol Sodium Succinate Injection

Category: Adrenocortical steroid.

Dose: By intravenous injection, the equivalent of 100 to 500 mg of hydrocortisone.

Usual strengths: The equivalent of 100 mg and 500 mg of hydrocortisone.

Standards: Hydrocortisone Sodium Succinate Injection is a suitably buffered sterile solution of hydrocortisone sodium succinate in Water for Injection. It is prepared by dissolving the contents of a sealed container in the requisite amount of Water for Injection immediately before use. The contents of the sealed container are made from Hydrocortisone Hydrogen Succinate with the help of a suitable alkali such as *sodium hydroxide* or *sodium carbonate.*

Content of hydrocortisone, $C_{21}H_{30}O_5$: Determine the weight of the contents of each of ten containers as described in the test for **Uniformity of weight** under Injections. From the result of the **Assay** calculate the proportionate amount of hydrocortisone, $C_{21}H_{30}O_5$, in each container. This amount does not deviate from the amount stated on the label by more than 7.5 per cent, except that in one container the amount may deviate by not more than 15.0 per cent.

Other requirements: Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements:

Description: White or almost white solid which yields a clear, colourless solution when dissolved in *water.*

Identification: (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar intensities to, those in the spectrum of *hydrocortisone sodium succinate R.S.,* Appendix 5.15B.

(B) Carry out the method for *thin-layer chromatography,* Appendix 5.4.3, using *silica gel G* as the coating substance and a freshly prepared mixture of 60 volumes of *n-butyl alcohol,* 20 volumes of *acetic anhydride* and 20 volumes of *water* as the mobile phase. Apply separately to the plate 2 μl of each of three solutions in *methyl alcohol* containing (1) 0.25 per cent w/v of the contents of the sealed containers; (2) 0.25 per cent w/v of *hydrocortisone sodium succinate R.S.* and (3) a mixture of equal volumes of solutions (1) and (2). After removal of the plate allow it to dry in air until the solvents have evaporated, spray with a 20 per cent w/v solution of *sulphuric acid* in *alcohol,* heat at 120° for ten minutes, allow to cool and examine under an ultra-violet lamp having a maximum output at about 365 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2) and the principal spot in the chromatogram obtained with solution (3) appears as a single compact spot.

pH: Between 6.5 and 8.0, determined in a solution containing the equivalent of 5.0 per cent w/v of hydrocortisone, Appendix 5.10

Related substances: Carry out the method for *thin-layer chromatography,* Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 77 volumes of *methylene chloride,* 15 volumes of *solvent ether,* 8 volumes of *methyl alcohol* and 1.2 volumes of *water* as the mobile phase. Apply separately to the plate 1 μl of each of the following solutions. Solution (1) contains 1.5 per cent w/v of the contents of the sealed container in *water.* Solution (2) contains 1.5 per cent w/v of *hydrocortisone sodium succinate R.S.* in *water.* Solutions (3) and (4) contain 0.105 per cent w/v of *hydrocortisone R.S.* and 0.030 per cent w/v of *hydrocortisone acetate R.S.* respectively in a mixture of equal volumes of *chloroform* and *methyl alcohol.* After removal of the plate allow it to dry in air until the solvents have evaporated. Heat at 105° for ten minutes, cool and spray with *alkaline tetrazolium blue solution.* The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (3). Any other secondary spot in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (4).

Stability of solution: A solution containing the equivalent of 5 per cent w/v of hydrocortisone remains clear when protected from light at about 20° for 48 hours.

Assay: Dissolve the mixed contents of ten containers in sufficient *water* to produce a solution containing the equivalent of 0.001 per cent w/v of hydrocortisone. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 248 nm, Appendix 5.15A. Calculate the content of $C_{21}H_{30}O_5$ taking 449 as the value of E(1 per cent, 1-cm) at the maximum at about 248 nm.

Storage: Store in a cool dry place. The constituted solution should be used immediately after preparation.

Labelling: The label on the sealed container states (1) the strength in terms of the equivalent of hydrocortisone; that (2) the prepared solution should be used only if it is clear; and (3) the solution should be discarded after 48 hours.

Hydroxypropylcellulose

Cellulose, 2-hydroxypropyl ether; Hyprolose

Category: Pharmaceutical aid (tablet excipient; suspending agent).

Description: White or yellowish-white powder; practically odourless; hygroscopic after drying.

Solubility: Soluble in *water*, in *ethyl alcohol*, in *methyl alcohol*, in *chloroform* and in *propylene glycol* forming colloidal solutions; slightly soluble in *acetone;* very slightly soluble in *toluene;* practically insoluble in hot *water.*

Standards: Hydroxypropylcellulose is a cellulose having some of the hydroxyl groups in the form of the 2-hydroxypropyl ether. The various grades available commercially are distinguished by the apparent viscosities of their 2 per cent w/v solution measured at 20°.

Identification: (A) With constant stirring add a quantity containing equivalent of 1.0 g of the dried substance into 50 ml of *carbon dioxide-free water* previously heated to 90°. Allow to cool, dilute to 100 ml with *carbon dioxide-free water* and continue stirring until solution is complete (solution A). Heat 10 ml of solution A on a water-bath with stirring. At temperatures above 40° the solution becomes cloudy or a flocculent precipitate is formed. On cooling the solution becomes clear.

(B) To 10 ml of solution A add 0.3 ml of *2N acetic acid* and 2.5 ml of a 10 per cent w/v solution of *tannic acid.* A yellowish-white, flocculent precipitate is produced which dissolves in *6N ammonia.*

(C) Without heating, completely dissolve 0.2 g in 15 ml of a 70 per cent of w/w solution of *sulphuric acid,* pour the solution with stirring into 100 ml of iced *water.* In a test-tube kept in ice, mix thoroughly 1 ml of the solution with 8 ml of *sulphuric acid,* added dropwise. Heat in a water-bath for exactly 3 minutes and cool immediately in ice. When the mixture is cool, carefully add 0.6 ml of a solution containing 3 g of *ninhydrin* in 100 ml of a 4.55 per cent w/v solution of *sodium metabisulphite,* mix well and allow to stand at 25°. A pink colour is produced immediately which becomes violet within 100 minutes.

(D) Place 1 ml of solution A on a glass plate. After evaporation of the water a thin film is produced.

pH: Between 5.0 and 8.5, determined in solution A, Appendix 5.10.

Apparent viscosity: Between 75 per cent and 140 per cent of the stated value, determined by the following method. Weigh accurately a quantity equivalent to 2 g of the dried substance and add with constant stirring to 50 ml of *water* previously heated to 90°. Allow to cool, dilute to 100 ml with *water* and continue stirring until the solution is complete. Determine the *viscosity* at 20° by Method C, Appendix 5.18, using a shear rate of $10\ s^{-1}$.

Heavy metals: Not more than 20 parts per million, determined by method B, Appendix 3.2.4.

Chloride: 15 ml of solution A complies with the *limit test for chlorides,* Appendix 3.2.2.

Sulphated ash: Not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying: Not more than 5.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Storage: Store in tightly-closed containers.

Labelling: The label on the container states the apparent viscosity in centipoises of a 2 per cent w/v solution. For products of low viscosity, the label also states the concentration of the solution satisfactory for use.

Hydroxypropylmethylcellulose

Cellulose, 2-hydroxypropylmethyl ether; Hypromellose

Category: Pharmaceutical aid (tablet excipient; suspending agent).

Description: White or yellowish-white, fibrous or granular powder; almost odourless.

Solubility: It swells in *water* forming an opalescent, viscous colloidal solution. Practically insoluble in hot *water*, in *ethyl alcohol*, in *chloroform* and in *solvent ether*.

Standards: Hydroxypropylmethylcellulose is a cellulose having some of the hydroxyl groups in the form of the methyl ether and some in the form of the 2-hydroxypropyl ether. The various grades available commercially are distinguished by the apparent viscosities of their 2 per cent w/v solutions measured at 20°.

Identification: (A) With constant stirring add a quantity containing the equivalent of 1.0 g of the dried substance into 50 ml of *carbon dioxide-free water* previously heated to 90°. Allow to cool, dilute to 100 ml with *carbon dioxide-free water* and continue stirring until solution is complete (solution A). Heat 10 ml of solution A on a water-bath with stirring. At temperatures above 50° the solution becomes cloudy or a flocculent precipitate is produced. On cooling the solution becomes clear or slightly opalescent.

(B) To 10 ml of solution A add 10 ml of *N sodium hydroxide* or *N hydrochloric acid;* in either case the mixture remains stable.

(C) Complies with **Identification** tests (B), (C) and (D) described under Hydroxypropylcellulose.

pH: Between 5.5 and 8.0, determined in solution A, Appendix 5.10.

Apparent viscosity, Heavy metals and Chloride: Complies with the requirements stated under Hydroxypropylcellulose.

Sulphated ash: Not more than 3.0 per cent, Appendix 3.2.7.

Loss on drying: Not more than 10.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Storage: Store in tightly-closed containers.

Labelling: The label on the container states the apparent viscosity in centipoises of a 2 per cent w/v solution.

Icing Sugar

Confectioner's Sugar

Category: Pharmaceutical aid.

Description: Fine, white, free-flowing powder; odourless; taste, sweet.

Standards: Icing Sugar is Sucrose ground together with Starch (maize) to a fine powder. It contains not less than 95.0 per cent of sucrose, $C_{12}H_{22}O_{11}$, calculated with reference to the dried substance.

Identification: Shake 2 g with 10 ml of *water* and filter. To the residue add 5 ml of *water*, mix and then boil for one minute. Cool and add one drop of *0.01N iodine;* a dark blue colour is produced. To the filtrate add 1 ml of *0.1N sulphuric acid* and boil. Cool, neutralise to *litmus paper* with *sodium hydroxide solution* and add 2 ml of *potassium cupri-tartrate solution* and boil; a copious red precipitate is produced.

Specific optical rotation: Not less than + 62.6°, determined in a solution prepared in the following manner. Weigh accurately about 20 g, add 80 ml of *water* and shake to dissolve the sucrose. Add sufficient water to produce 100.0 ml, mix well and filter, discarding the first few ml of the filtrate, Appendix 5.12.

Chloride: To 10 ml of the filtrate obtained in the test for **Specific optical rotation** add 10 ml of *dilute nitric acid*, 30 ml of *water* and 1 ml of *silver nitrate solution;* the opalescence produced is not greater than that produced by 0.40 ml of *0.02N hydrochloric acid* treated in the same manner.

Sulphate: To 25 ml of the filtrate obtained in the test for **Specific optical rotation** add 2 ml of *dilute hydrochloric acid*, 20 ml of *water* and 2 ml of *barium chloride solution;* the opalescence produced is not greater than that produced by 0.30 ml of *0.02N sulphuric acid* treated in the same manner.

Calcium: To 5 ml of the filtrate obtained in the test for **Specific optical rotation** add 5 ml of *water* and 1 ml of *ammonium oxalate solution;* the solution remains clear for not less than a minute.

Heavy metals: Not more than 5 parts per million, determined by Method A on a solution prepared in the following manner. To 20 ml of the filtrate obtained in the test for **Specific optical rotation** add 4 ml of *water* and 1 ml of *0.1N hydrochloric acid,* Appendix 3.2.4.

Microbial limits: 1 g meets the requirements of the test for absence of *E. coli* and *salmonellae,* Appendix 4.5.

Sulphated ash: Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying: Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105° for 4 hours, Appendix 5.8.

Assay: Calculate the *specific optical rotation* with reference to the dried substance and calculate the content of $C_{12}H_{22}O_{11}$ as a percentage from the expression

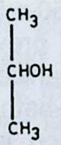
$$D\times 100/65.9$$

in which D is the specific optical rotation.

Storage: Store in well-closed containers.

Isopropyl Alcohol

Propan-2-ol



$CH_3CH(OH)CH_3$

C_3H_8O Mol. Wt. 60.10

Category: Pharmaceutical aid (solvent).

Description: Clear, colourless liquid; odour, characteristic and spirituous. Flammable.

Solubility: Miscible with *water,* with *chloroform* and with *solvent ether.*

Standards: Isopropyl Alcohol is propan-2-ol.

Identification: (A) Mix 1 ml of a 10 per cent v/v solution with 2 ml of *mercuric sulphate solution* and heat just to boiling; a white or yellowish-white precipitate is produced.

(B) Heat 1 ml gently with 4 ml of *potassium dichromate solution* and 1 ml of *sulphuric acid;* acetone, recognisable by its characteristic odour, is evolved.

Wt. per ml: Between 0.783 and 0.787 g, Appendix 5.19.

Refractive index: Between 1.377 and 1.378, determined at 20°, Appendix 5.14.

Distillation range: Not less than 95.0 per cent v/v distils between 81° and 83°, Appendix 5.3.

Acidity or alkalinity: Boil 25 ml gently for five minutes with 25 ml of *carbon dioxide-free water* and cool with precautions to exclude carbon dioxide; the solution is not alkaline to *phenolphthalein solution* and requires not more than 0.06 ml of *0.1N sodium hydroxide* to make it alkaline.

Aldehydes and ketones: Mix in a cylinder 25 ml with 25 ml of *water* and 50 ml of *hydroxylamine hydrochloride solution,* allow to stand for five minutes and titrate with *0.1N sodium hydroxide* until the colour matches that of 50 ml of *hydroxylamine hydrochloride solution* contained in a similar cylinder, each being viewed down the axis of the cylinder. Not more than 2.0 ml of *0.1N sodium hydxoxide* is required.

Water-insoluble matter: Mix one volume with 19 volumes of *water;* no opalescence is produced.

Non-volatile matter: Not more than 0.005 per cent w/v, determined on 100 ml by evaporating and drying at 105°.

Water: Not more than 0.50 per cent w/w; Appendix 3.3.25.

Storage: Store in tightly-closed containers.

Mannitol Injection

Mannitol Intravenous Infusion

Category: Diuretic; diagnostic aid (renal function determination).

Dose: *Diuretic*—Mannitol, by intravenous infusion, 50 to 100 g daily but not more than 50 g on one occasion in a 5 to 20 per cent w/v solution.

Diagnostic aid—Mannitol, by intravenous infusion, 0.2 g per kg of body weight in a 15 to 25 per cent w/v solution.

Usual strengths: Intravenous infusions containing 10.0, 15.0, 20.0, and 25.0 per cent w/v of Mannitol.

Standards: Mannitol Injection is a sterile solution of Mannitol in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_6H_{14}O_6$.

Description: Colourless or almost colourless clear solution.

Identification: (A) Evaporate to dryness on a water-bath a volume equivalent to 2.0 g of Mannitol. The residue melts at about 167°, Appendix 5.11.

(B) The residue obtained in **Identification** test (A) complies with **Identification** tests (A) and (B) described under Mannitol.

pH: Between 4.5 and 7.0, Appendix 5.10, determined in a solution containing not more than 10.0 per cent w/v of Mannitol, diluted if necessary with *water* and to which 0.3 ml of a saturated solution of *potassium chloride* has been added for each 100 ml of solution.

Pyrogens: Complies with the *test for pyrogens*, Appendix 2.36, using a quantity containing the equivalent of not less than 0.5 g of Mannitol per kg of the rabbit's weight.

Other requirements: Complies with the requirements stated under Injections.

Assay: Dilute a volume equivalent to 0.4 g of Mannitol to 100.0 ml with *water*, transfer 10.0 ml to a stoppered flask, add 20.0 ml of a 2.14 per cent w/v solution of *sodium periodate* and 2 ml of *dilute sulphuric acid* and heat on a water-bath for fifteen minutes. Cool, add 3.0 g of *sodium bicarbonate* and 25.0 ml of *0.2N sodium arsenite*, mix, and add 5 ml of a 20 per cent w/v solution of *potassium iodide* and allow to stand for fifteen minutes. Titrate with *0.1N iodine* until the first trace of yellow colour appears. Repeat the operation without the substance being examined; the difference between the titrations represents the amount of *0.1N iodine* required. Each ml of *0.1N iodine* is equivalent to 0.001822 g of $C_6H_{14}O_6$.

Storage: Store at a temperature between 20° and 30°. Exposure to lower temperatures may cause the deposition of crystals, which should be dissolved by warming before use.

Labelling: The label on the container states (1) the strength as a percentage w/v of Mannitol; (2) the storage conditions; (3) the date after which the injection is not intended to be used; and (4) that the injection should not be used if it contains visible solid particles.

Methylcellulose

Cellulose methyl ether

Category: Pharmaceutical aid (tablet excipient; suspending agent) and bulk-forming laxative.

Description: White, yellowish-white or greyish-white powder or granules; practically odourless; tasteless.

Solubility: Practically insoluble in hot *water*, in *ethyl alcohol*, in *acetone*, in *solvent ether* and in *toluene*. It forms a colloidal solution in cold *water*.

Standards: Methylcellulose is a methyl ether of cellulose. It contains not less than 27.5 per cent and not more than 31.5 per cent of methoxy ($-OCH_3$) groups, calculated with reference to the dried substance.

Identification, pH, Heavy metals and Chloride: Complies with the requirements stated under Hydroxypropylcellulose.

Apparent viscosity: Not less than 80.0 per cent and not more than 120.0 per cent of the stated value for viscosity types of 100 centipoises or less; and not less than 75.0 per cent and not more than 140.0 per cent of the stated value for viscosity types of more than 100 centipoises; determined on a 2.0 per cent w/w solution by the following method. Transfer 2.0 g, accurately weighed, calculated with reference to the dried substance, to a 250-ml wide-mouth centrifuge tube, add 98 g of *water* previously heated to about 90° and stir with a mechanical stirrer for 10 minutes. Place the tube in ice-bath, continue stirring for 40 minutes or till solution is complete. Adjust the weight of the solution to 100 g, if necessary, and centrifuge the solution to remove entrapped air. Determine the *viscosity* at 20° by Method C, Appendix 5.18.

Sulphated ash: Not more than 1.0 per cent, Appendix 3.2.7.

Loss on drying: Not more than 5.0 per cent, determined on 1.0 g by drying in an oven at 105° for 2 hours, Appendix 5.8.

Assay: Weigh accurately about 50 mg in an empty, tared Hard Gelatin Capsule Shell and place the capsule and contents in the boiling flask of the apparatus in the method for the *determination of methoxyl*, Appendix 3.3.3. Proceed as directed in the appendix. Each ml of *0.1N sodium thiosulphate* is equivalent to 0.0005172 g of methoxy ($-OCH_3$) groups.

Storage: Store in well-closed containers.

Labelling: The label on the container states the apparent viscosity in centipoises of a 2.0 per cent w/w solution.

Methylene Chloride

Dichloromethane

CH_2Cl_2 **Mol. Wt. 84.93**

Category: Pharmaceutical aid (solvent).

Description: Clear, colourless; mobile liquid, having an odour resembling that of chloroform.

Solubility: Miscible with *alcohol*, with *solvent ether* and with fixed and volatile oils.

Specific gravity: Between 1.318 and 1.322, Appendix 5.19.

Distillation range: Not less than 95.0 per cent distils between 39° and 41°, Appendix 5.3.

Free chlorine: To 10 ml add 10 ml of *water*, 0.1 ml of *starch solution* and 0.1 ml of *potassium iodide solution*, shake for 2 minutes and allow the liquids to separate. The lower layer does not show a violet tint.

Hydrogen chloride: Into each of two glass-stoppered cylinders place 10 ml of *water*, 2 drops of *phenolphthalein solution* and sufficient *0.01N sodium hydroxide* to produce a pink colour that persists after vigorously shaking for 30 seconds, and is of equal intensity in each cylinder. (Note: In the following steps take special care to avoid contamination with carbon dioxide). Into one of the cylinders place 20.0 ml of methylene chloride and 0.70 ml of *0.01N sodium hydroxide* and again shake well. The pink colour in the test cylinder is at least as intense as that in the comparison cylinder, and the colour persists for not less than 15 minutes.

Heavy metals: Not more than 1 part per million, determined in a solution prepared by evaporating 15 ml (20 g) in a glass evaporating dish on a water-bath to dryness, cooling, adding 2 ml of *hydrochloric acid*, slowly evaporating again on a water-bath to dryness, cooling and dissolving in 1 ml of *N acetic acid* and 24 ml of *water* and proceeding as described under Method A, Appendix 3.2.4.

Non-volatile residue: Not more than 0.002 per cent w/w, determined on 50 g by evaporating in a platinum or porcelain dish on a water-bath and drying at 105° for 30 minutes.

Water: Not more than 0.05 per cent w/w, Appendix 3.3.25.

Storage: Store in tightly-closed containers in a cool place.

NOTE— Perform all operations involving evaporation of methylene chloride in a well-ventilated hood.

Metoclopramide Syrup

Metoclopramide Hydrochloride Syrup

Category: Antiemetic; accelerator of gastric emptying.

Dose: The equivalent of 10 to 30 mg of anhydrous metoclopramide hydrochloride daily, in divided doses.

Usual strength: The equivalent of 5 mg of anhydrous metoclopramide hydrochloride in 5 ml.

Standards: Metoclopramide Syrup contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of metoclopramide hydrochloride, $C_{14}H_{22}ClN_3O_2,HCl$.

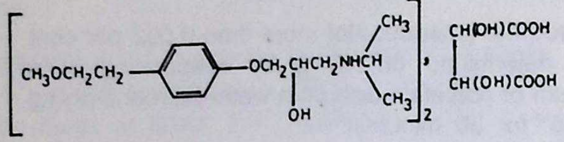
Identification: To 50 ml add *sodium hydroxide solution* till alkaline and extract with three quantities, each of 40 ml of *chloroform*, dry each extract with *anhydrous sodium sulphate*. Evaporate the combined extracts to dryness on a water-bath. The residue complies with **Identification** tests (B) and (C) described under Metoclopramide Hydrochloride.

pH: Between 2.0 and 4.0, Appendix 5.10

Assay: Dilute an accurately measured volume equivalent to 10 mg of anhydrous metoclopromide hydrochloride to 100.0 ml with *water*, and complete the **Assay** described under Metoclopramide Injection, beginning at the words "To 20.0 ml add........"

Storage: Store in well-closed, light-resistant containers.

Metoprolol Tartrate



$(C_{15}H_{25}NO_3)_2,C_4H_6O_6$ Mol. Wt. 684.82

Category: ß-Receptor antagonist (antihypertensive; antianginal; antiarrhythmic).

Dose: 100 to 450 mg daily, in divided doses; the initial dose should not exceed 100 mg daily.

Description: White, crystalline powder.

Solubility: Insoluble in *solvent ether;* slightly soluble in *acetone;* freely soluble in *methylene chloride,* in *chloroform* and in *alcohol;* very soluble in *water.*

Standards: Metoprolol Tartrate is 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]-2-propanol, (±)-,[*R*-(**R*,*R**)]-2,3-dihydroxybutanedioate (2:1) (salt). It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $(C_{15}H_{25}NO_3)_2$, $C_4H_6O_6$, calculated with reference to the dried substance.

Identification: The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *metoprolol tartrate R.S.,* Appendix 5.15B.

Specific optical rotation: Between +6.5° and +10.5°, determined at 20° in a 2.0 per cent w/v solution, Appendix 5.12.

pH: Between 6.0 and 7.0, determined in a 10.0 per cent w/v solution, Appendix 5.10.

Heavy metals: Not more than 10 parts per million, determined by method A, Appendix 3.2.4.

Related substances: Carry out the method for *thin-layer chromtography,* Appendix 5.4.3, using *silica gel* G as the coating substance and *chloroform* as the mobile phase. Pour 200 ml of *chloroform* in the developing chamber containing several beakers, each containing 45 ml of *strong ammonia solution* and saturate for one and a half hours by lining the walls with absorbent paper. Apply separately to the plate 5 μl of each of two solutions in *chloroform* containing (1) 2.0 per cent w/v of the substance being examined, and (2) 0.02 per cent w/v of *metoprolol tartrate R.S.* After removal of the plate, dry it in a current of warm air until the odour of ammonia is no longer perceptible. Place the plate in a chamber of chlorine gas prepared by adding 5 ml of *5N hydrochloric acid* to a beaker containing 0.5 g of *potassium permanganate,* and let the plate remain in the chamber for about a minute. Remove the plate from the chamber, allow to stand for a few minutes and spray with *alcoholic potassium iodide-starch solution.* Any spot, other than the principal spot, in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash: Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying: Not more than 0.5 per cent, determined on 1.0 g by drying 'in vacuo at 60°' for four hours, Appendix 5.8.

Assay: Weigh accurately about 0.3 g, dissolve in 30 ml of *glacial acetic acid* and titrate with *0.1N perchloric acid,* using two drops of *crystal violet solution* as indicator. Carry out a blank determination and make necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03424 g of $(C_{15}H_{25}NO_3)_2,C_4H_6O_4$.

Storage: Store in tightly-closed, light-resistant containers.

Metoprolol Tartrate Tablets

Category: ß-Receptor antagonist (antihypertensive; antianginal; antiarrhythmic).

Dose: Metoprolol Tartrate, 100 to 450 mg daily, in divided doses; the initial dose should not exceed 100 mg daily.

Usual strengths: 50 mg; 100 mg.

Standards: Metoprolol Tartrate Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Metoprolol Tartrate, $(C_{15}H_{25}NO_3)_2,C_4H_6O_6$.

Identification: Weigh a quantity of the powdered tablets equivalent to about 40 mg of Metoprolol Tartrate, transfer to a separator and add 25 ml of *water* and 4 ml of *dilute ammonia solution.* Extract with 20 ml of *chloroform,* filtering the chloroform extract through *anhydrous sodium sulphate,* previously rinsed with *chloroform.* Evaporate the chloroform extract to dryness and place in a freezer to congeal the residue. The *infra-red absorption spectrum* of a potassium bromide dispersion of the residue so obtained exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *metoprolol tartrate R.S* treated in the same manner, Appendix 5.15B.

Dissolution: Comply with the *dissolution test for tablets and capsules,* Appendix 5.7, using as medium 900 ml of *simulated gastric juice* (without pepsin) and placing one tablet in the basket for each test and rotating the basket for 30 minutes. Withdraw a sample of about 10 ml of the medium and filter. Measure the *extinction* of the filtrate, suitably diluted, if necessary, at the maximum at about 275 nm, Appendix 5.15A. Calculate the content of $(C_{15}H_{25}NO_3)_2,C_4H_6O_6$ in the medium from the *extinction* obtained from a solution of known concentration of *metoprolol tartrate R.S.* in the same medium. The amount of metoprolol tartrate in the solution is not less than 75 per cent of the stated amount.

Other requirements: Comply with the requirements stated under Tablets.

Assay: Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.12 g of Metoprolol Tartrate, transfer to a 100-ml volumetric flask, add about 75 ml of *alcohol* and shake for 15 minutes. Dilute to volume with *alcohol,* mix and filter. Discard the first 10 ml of the filtrate and dilute 5.0 ml of the filtrate to 50.0 ml with *alcohol.* Measure the *extinction* of a l-cm layer of the resulting solution at the maximum at about 275 nm, using *alcohol* as the blank, Appendix 5.15A. Calculate the content of $(C_{15}H_{25}NO_3)_2,C_4H_6O_6$ from the *extinction* obtained by repeating the operation using *metoprolol tartrate R.S.* instead of the substance being examined and from the declared content of $(C_{15}H_{25}NO_3)_2,C_4H_6O_6$ in the *metoprolol tartrate R.S.*

Storage: Store in tightly-closed, light-resistant containers.

Metronidazole Benzoate Oral Suspension

Benzoyl Metronidazole Oral Suspension

Category: Anti-amoebic.

Dose: For amoebic dysentry, the equivalent of 400 mg of metronidazole thrice daily, for 5 to 10 days.

NOTE—200 mg of Metronidazole Benzoate is approximately equivalent to 125 mg of metronidazole.

Usual strength: The equivalent of 100 mg of metronidazole in 5 ml.

Standards: Metronidazole Benzoate Oral Suspension contains a quantity of Metronidazole Benzoate equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of metronidazole, $C_6H_9N_3O_3$. It may contain suitable colouring, flavouring, sweetening, buffering and suspending agents and antimicrobial agents.

Identification: Extract a quantity of the suspension equivalent to 0.5 g of metronidazole with *chloroform,* filter and evaporate the filtrate to dryness. The residue complies with the **Identification** tests and the test for **Melting range** described under Metronidazole Benzoate.

Assay: Weigh accurately a quantity equivalent to 200 mg of metronidazole, add 10 ml of *water* and extract with four quantities, each of 25 ml, of *chloroform.* Combine the chloroform extracts and wash with two quantities, each of 5 ml, of *water.* Wash the aqueous solution with 5 ml of *chloroform* and evaporate the combined chloroform extracts and washing to dryness on a water-bath. Add two successive quantities of *acetone* and complete the **Assay** described under Metronidazole Benzoate, beginning at the words "Add 10 ml of *acetic anhydride* ....". Each ml of *0.1N perchloric acid* is equivalent to 0.01712 g of $C_6H_9N_3O_3$. Determine the weight per ml of the suspension and calculate the content of metronidazole, weight in volume.

Storage: Store in tightly-closed, light-resistant containers.

Labelling: The label on the container states the strength in terms of the equivalent amount of metronidazole in a suitable dose-volume.

Metronidazole Injection

Metronidazole Intravenous Infusion

Category: Antibacterial (anaerobic).

Dose: Metronidazole. Initial dose, by intravenous infusion, 15 mg per kg of body weight; subsequent doses, 7.5 mg per kg of body weight upto a maximum of 1 g every six hours for seven days or longer.

Usual strength: 5 mg per ml.

Standards: Metronidazole Injection is a sterile solution of Metronidazole in Water for Injection. It contains not less than 90.00 per cent and not more than 110.0 per cent of the stated amount of $C_6H_9N_3O_3$. It may contain suitable buffering agents.

Description: Clear, colourless or faintly straw-coloured liquid.

Identification: (A) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 70 volumes of *chloroform*, 28 volumes of *methyl alcohol*, 4 volumes of *water* and 2 volumes of *strong ammonia solution* as the mobile phase. Apply separately to the plate 5 μl of each of the following solutions. For solution (1) use a volume of the injection equivalent to 0.025 mg of Metronidazole; solution (2) is a 0.5 per cent w/v solution of *metronidazole R.S.* After removal of the plate allow it to dry in air until the odour of the solvents is not detectable and examine under an ultra-violet lamp having a maximum output at about 254 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

(B) Heat 2 ml in a water-bath for five minutes with 10 mg of *zinc powder* and 0.25 ml of *hydrochloric acid,* cool in ice, add 0.5 ml of *sodium nitrite solution* and remove the excess of nitrite with *sulphamic acid.* Add 0.5 ml of the product to a mixture of 0.5 ml of *ß-naphthol solution;* an orange-red colour is produced.

pH: Between 4.5 and 7.0, Appendix 5.10.

Pyrogens: Complies with the *test for pyrogens,* Appendix 2.36, using a volume equivalent to 15 mg of Metronidazole per kg of the rabbit's weight.

Other requirements: Complies with the requirements stated under Injections.

Assay: Dilute a suitable volume with sufficient *0.1N hydrochloric acid* to produce a solution containing 0.001 per cent w/v of Metronidazole. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 277 nm, Appendix 5.15A, using as blank a solution prepared in the same manner omitting the substance being examined. Calculate the content of $C_6H_9N_3O_3$ from the *extinction* obtained by repeating the operation using *metronidazole R.S.* instead of the substance being examined, and from the declared content of $C_6H_9N_3O_3$ in the *metronidazole R.S.*

Storage: Store in single-dose, light-resistant containers.

Labelling: The label on the container states (1) the date after which the injection is not intended to be used; (2) that the contents should not be used if they contain visible solid particles; and (3) the storage conditions.

Miconazole Ointment

Miconazole Nitrate Ointment

Category: Antifungal (topical)

Usual strength: 2 per cent w/w.

Standards: Miconazole Ointment contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Miconazole Nitrate, $C_{18}H_{14}Cl_4N_2O,HNO_3$.

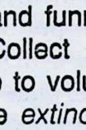
Identification: To a quantity containing 40 mg of Miconazole Nitrate add 20 ml of a mixture of 1 volume of *2N sulphuric acid* and 4 volumes of *methyl alcohol* and mix; shake with two quantities, each of 50 ml, of *carbon tetrachloride* and discard the organic layers. To the aqueous phase add sufficient *dilute ammonia solution* to make it alkaline and extract with two quantities, each of 40 ml, of *chloroform.* Combine the chloroform extracts, shake with *anhydrous sodium sulphate,* filter and dilute the filtrate to 100 ml with *chloroform.* Evaporate 50 ml to dryness and dissolve the residue in 50 ml of a mixture of 1 volume of *0.1N hydrochloric acid* and 9 volumes of *methyl alcohol.* The light absorption of the resulting solution, in the range 230 to 350 nm, exhibits maxima at about 264, 272 and 280 nm; the ratio of the *extinction* at 264 nm to that at 280 nm is about 0.8, Appendix 5.15A.

Assay: Weigh accurately a quantity equivalent to 0.1 g of Miconazole Nitrate and dissolve in sufficient quantity of a mixture of equal volumes of *isopropyl alcohol* and *chloroform* to produce 100.0 ml. Pipette 25.0 ml of this solution into a beaker and evaporate to dryness on a water-bath with the aid of a current of nitrogen. Add 10 ml of *chloroform* to the residue and heat on a water-bath just to boiling, stir well and cool. Add 50 ml of *pentane* in small quantities with continuous stirring. Allow to crystallise for ten to fifteen minutes. Filter through a sintered-glass funnel, wash the beaker with four quantities, each of 5 ml, of *pentane* and add the washings to the filter funnel. Wash the funnel and precipitate with four quantities, each of 5 ml, of *pentane.* Dry the precipitate on the filter by passing air through it and dissolve it by washing the beaker and funnel with small quantities of *methyl alcohol.* Collect the filtrate in a 50-ml graduated flask, dilute to volume with *methyl alcohol* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 271 nm, Appendix 5.15A, using *methyl alcohol* as the blank. Calculate the content of $C_{18}H_{14}Cl_4N_2O, HNO_3$ from the *extinction* obtained with a 0.05 per cent w/v solution of *miconazole nitrate R.S.* in *methyl alcohol* and from the declared content of $C_{18}H_{14}Cl_4N_2O,HNO_3$ in the *miconazole nitrate R.S.*

Storage: Store in tightly-closed containers in a cool place.

Monothioglycerol

Thioglycerol



$$\begin{array}{c} CH_2OH \\ | \\ CHOH \\ | \\ CH_2SH \end{array}$$

$C_3H_8O_2S$ Mol. Wt. 108.15

Category: Pharmaceutical aid.

Description: Colourless or pale yellow, viscous, hygroscopic liquid; odour resembling that of sulphides.

Solubility: Freely soluble in *water,* miscible with *alcohol;* insoluble in *solvent ether.*

Standards: Monothioglycerol is 3-mercapto-1,2-propanediol. It contains not less than 97.0 per cent and not more than the equivalent of 101.0 per cent of $C_3H_8O_2S$, calculated with reference to the anhydrous substance.

Specific gravity: Between 1.241 and 1.250, Appendix 5.19.

Refractive index: Between 1.521 and 1.526, Appendix 5.14.

pH: Between 3.5 and 7.0, determined in a 10.0 per cent w/v solution, Appendix 5.10.

Heavy metals: Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

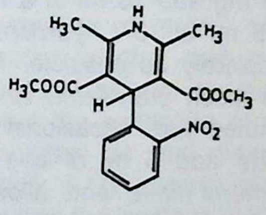
Sulphated ash: Not more than 0.1 per cent, Appendix 3.2.7.

Water: Not more than 5.0 per cent w/v, determined on 50 g, Appendix 5.20.

Assay: Weigh accurately about 0.4 g and dissolve in 50 ml of *water.* Titrate with *0.1N iodine,* adding 3 ml of *starch solution* towards the end of the titration. Each ml of *0.1N iodine* is equivalent to 0.01082 g of $C_3H_8O_2S$.

Storage: Store in tightly-closed containers.

Nifedipine



$C_{17}H_{18}N_2O_6$ Mol. Wt. 346.34

Category: Coronary vasodilator; antianginal.

Dose: Initial dose, up to 30 mg daily, in divided doses; subsequent doses, in accordance with the needs of the patient but total daily dose not to exceed 100 mg.

Description: Yellow powder; affected by exposure to light.

Solubility: Practically insoluble in *water;* freely soluble in *acetone* and in *chloroform.*

Standards: Nifedipine is dimethyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-pyridine-3,5-dicarboxylate. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{17}H_{18}N_2O_6$, calculated with reference to the dried substance.

NOTE—Nifedipine, when exposed to daylight and certain wavelengths of artificial light, readily converts to a nitrosophenyl pyridine derivative. Exposure to ultra-violet light leads to the formation of a nitrophenyl pyridine derivative. Perform the tests and assays in the dark or under special fluorescent light. Use low-actinic glassware.

Identification: (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *nifedipine R.S.*, Appendix 5.15B.

(B) Dissolve about 70 mg in 5 ml of *chloroform* and add sufficient *methyl alcohol* to produce 50.0 ml. Dilute 1.0 ml of this solution to 100.0 ml with *methyl alcohol.* The light absorption, in the range 230 to 350 nm, of a 1-cm layer of the resulting solution with *methyl alcohol* as the blank, exhibits maxima and minima at the same wavelengths as that of a solution of *nifedipine R.S.* prepared in the same manner, Appendix 5.15A.

(C) The ratio of the *extinction* of a 1-cm layer of the diluted solution in *methyl alcohol,* described in the **Assay,** at 350 nm to that at 250 nm is not less than 1.48 and not more than 1.65.

(D) To about 50 mg add 10 ml of a mixture of 5 ml of *alcohol* and 5 ml of *3N hydrochloric acid,* and dissolve as completely as possible. To the solution add 0.5 g of 20 mesh *granulated zinc* and allow to stand for 5 minutes with occasional swirling. Filter and to the filtrate add 5 ml of a 1 per cent w/v solution of *sodium nitrite* and allow to stand for 2 minutes. Add 2 ml of a 5 per cent w/v solution of *ammonium sulphamate,* shake vigorously with care, and add 2 ml of a 0.5 per cent w/v solution of *N-(1-naphthyl)ethylenediamine hydrochloride;* an intense red colour develops which persists for not less than 5 minutes.

Melting range: Between 171° and 175°, Appendix 5.11.

Heavy metals: Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Chloride: To 5 g add 4 ml of *6N acetic acid* and 40 ml of water. Boil carefully, cool and filter through chloride and sulphate-free paper. Pass small quantities of *water* through the filter and combine the filtrate and washings. Add sufficient *water* to produce 50.0 ml (solution A). 6.0 ml of solution A complies with the *limit test for chlorides,* Appendix 3.2.2.

Sulphate: 12.0 ml of solution A complies with the *limit test for sulphates,* Appendix 3.2.8.

Related substances: Carry out the method for *thin-layer chromatography,* Appendix 5.4.3, using *silica gel G* as the coating substance and *isopropyl ether* as the mobile phase. Apply separately to the plate 10 μl of each of three solutions in *chloroform* containing (1) 5.0 per cent w/v of the substance being examined; (2) 0.01 per cent w/v of *dimethyl 4-(2-nitrophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate R.S.* and (3) 0.01 per cent w/v of *dimethyl 4-(2-nitrosophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate R.S.* Place the plate in an unsaturated chromatographic chamber covered with a black cloth during the development. After removal of the plate, allow it to dry in air until the odour of solvent is not detectable and examine under an ultra-violet lamp having a maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spots in the chromatograms obtained with solutions (2) and (3).

Sulphated ash: Not more than 0.1 per cent, determined on 1 g and by ignition at 600°, Appendix 3.2.7.

Loss on drying: Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay: Weigh accurately about 0.1 g, dissolve in 5 ml of *chloroform* and add sufficient *methyl alcohol* to produce 100.0 ml. To 5.0 ml of this solution add sufficient *methyl alcohol* to produce 100.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 350 nm, Appendix 5.15A, using *methyl alcohol* as the blank. Calculate the content of $C_{17}H_{18}N_2O_6$ from the *extinction* obtained by repeating the operation using *nifedipine R.S.* instead of the substance being examined, and from the declared content of $C_{17}H_{18}N_2O_6$ in the *nifedipine R.S.*

Storage: Store in tightly-closed, light-resistant containers.

Nifedipine Capsules

Category: Coronary vasodilator; antianginal.

Dose: Nifedipine. Initial dose, up to 30 mg daily, in divided doses; subsequent doses, in accordance with the needs of the patient, but total daily dose not to exceed 100 mg.

Usual strength: 10 mg.

Standards: Nifedipine Capsules contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Nifedipine, $C_{17}H_{18}N_2O_6$.

NOTE—Perform all the tests and assays in the dark or under special fluorescent light. Use low-actinic glassware.

Identification: Carry out the method for *thin-layer chromatography*, Appendix 5.4.3., using a 0.5-mm thick layer of *silica gel G* as the coating substance and a mixture of equal volumes of *ethyl acetate* and *cyclohexane* as the mobile phase. Apply separately to the plate 0.5 ml of each the following solutions in the form of 5-cm bands across the plate. For solution (1) transfer the contents of one capsule completely to a centrifuge tube, rinsing with about 10 ml of *sodium hydroxide solution*, extract with 10 ml of *methylene chloride* and centrifuge for ten minutes at 2000 to 5000 rpm; use the clear solvent layer. Solution (2) is a 0.12 per cent w/v solution of *nifedipine R.S.* and solution (3) is a mixture of equal volumes of solutions (1) and (2). Place the plate in the chromatographic chamber covered with a black cloth during the development of the chromatogram. After removal of the plate, allow it to dry in air until the odour of solvent is not detectable and examine under an ultra-violet lamp having a maximum output at about 254 nm. The principal band obtained in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2) and the principal band in the chromatogram obtained with solution (3) appears as a compact single band.

Related substances: Comply with the test described under Nifedipine, applying separately to the plate 20 µl of solution (1), 16 µl of solution (2) and 4 µl of solution (3). For solution (1) transfer the contents of 4 capsules completely to a centrifuge tube, add 8.4 ml of a mixture of equal volumes of *methylene chloride* and *methyl alcohol*, shake vigorously for ten minutes and centrifuge for ten minutes at 2000 to 5000 rpm. Solutions (2) and (3) are prepared as described in the test for **Related substances** under Nifedipine.

Uniformity of content: Transfer the contents of a capsule quantitatively to a 200-ml volumetric flask with the aid of small quantities of *methyl alcohol*, dilute to volume with *methyl alcohol* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 350 nm, Appendix 5.15A, using *methyl alcohol* as the blank. Calculate the content of $C_{17}H_{18}N_2O_6$ in the capsule from the *extinction* obtained with a 0.005 per cent w/v solution of *nifedipine R.S.* in *methyl alcohol* and from the declared content of $C_{17}H_{18}N_2O_6$ in the *nifedipine R.S.*

Repeat the operation with a further nine capsules and calculate the average content of the ten capsules. The content of each capsule is between 85 per cent and 115 per cent of the average except that for one capsule the content may be between 75 per cent and 125 per cent of the average.

Other requirements: Comply with the requirements stated under Capsules.

Assay: Transfer the contents of 5 capsules quantitatively to a 200-ml volumetric flask with the aid of small quantities of *methyl alcohol*, dilute to volume with *methyl alcohol* and mix. To 20.0 ml add sufficient *methyl alcohol* to produce 100.0 ml and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 350 nm, Appendix 5.15A, using *methyl alcohol* as the blank. Calculate the content of $C_{17}H_{18}N_2O_6$ from the *extinction* obtained with a 0.005 per cent w/v solution of *nifedipine R.S.* in *methyl alcohol* and from the declared content of $C_{17}H_{18}N_2O_6$ in the *nifedipine R.S.*

Storage: Store in tightly-closed, light-resistant containers.

Oral Rehydration Salts

ORS Powder

Category: Replacement solution for diarrhoeal dehydration.

Usual strengths: Oral Rehydration Salts-A, commonly used in India in the treatment of noncholeraic diarrhoea; Oral Rehydration Salts-Bicarbonate and Oral Rehydration Salts-Citrate, recommended by the World Health Organisation (WHO) and the United Nations Children's Fund (UNICEF), in amounts to be dissolved in the stated amounts of water. (For the formulas see under **Standards)**

Description: White to creamy-white, amorphous or crystalline powder with sweet taste.

Standards: Oral Rehydration Salts are a homogeneous mixture of Dextrose, Sodium Chloride, Potassium Chloride and either Sodium Bicarbonate or Sodium Citrate for use in oral rehydration therapy after being dissolved in the requisite amount of water. They may contain suitable flavouring agents and, where necessary, suitable flow agents in the minimum quantity required to achieve a satisfactory product. They contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amounts of Dextrose (anhydrous or monohydrate, as appropriate) and of the requisite amounts of sodium, Na^+, potassium, K^+, chloride, Cl^-, and bicarbonate, HCO_3^-, or citrate, $C_6H_5O_7^{-3}$ (as appropriate), calculated from the stated amounts of the relevant constituents.

The compositions of the three formulations are described below in terms of the amount in g to be dissolved in sufficient water to produce 1000 ml.

	Formula (g/l)		
	ORS-A	ORS-Bicarbonate	ORS-Citrate
Sodium Chloride	1.25	3.5	3.5
Potassium Chloride	1.5	1.5	1.5
Sodium Bicarbonate	—	2.5**	—
Sodium Citrate	2.9*	—	2.9
Anhydrous Dextrose or	36.4	20.0	20.0
Dextrose Monohydrate	40.0	22.0***	

* Sodium Bicarbonate (2.5 g/l) may be used in place of Sodium Citrate.

** Sodium Bicarbonate may be packaged separately.

*** Dextrose Monohydrate may be used when the Sodium Bicarbonate is packaged separately.

Identification: (A) When heated, melting and charring occurs and an odour of burnt sugar is produced.

(B) Add a few drops of the solution prepared as directed in the label to 5 ml of *potassium cupri-tartrate solution*; a copious red precipitate is produced on boiling.

(C) They give reactions A of *sodium*, of *potassium* and of *chlorides*, Appendix 3.1.

(D) Preparations containing Sodium Bicarbonate: To 5 g in a test-tube add 2 ml of *hydrochloric acid*; a vigorous effervescence is produced.

(E) Preparations containing Sodium Citrate: A quantity equivalent to about 50 mg of citric acid gives the reactions of *citrates*, Appendix 3.1.

Uniformity of weight: Weigh the contents of 10 randomly selected containers individually and determine the average weight. It is not less than the stated amount and the weight of contents of any single container is not less than 95 per cent and not more than 105 per cent of the stated amount. If the contents of not more than one container are less than 95 per cent but not less 90 per cent of the stated amount or more than 105 per cent but not more than 110 per cent of the stated amount, determine the weight of contents of 20 additional containers. The average weight of the contents of the 30 containers is not less than the stated amount, and the weight of contents of not more than one of the 30 containers is less than 95 per cent but not less than 90 per cent of the stated amount or more than 105 per cent but not more than 110 per cent of the stated amount.

Assay: Carry out the following assays on the well-mixed contents of an individual sachet or on a suitable sample from the well-mixed contents of a bulk container. Where the amount in an individual sachet is insufficient to carry out all the assays, take a separate sachet for the **Assay** for citrate and for the **Assay** for dextrose. For the **Assays** for sodium, for potassium, for chloride and for bicarbonate weigh accurately about 8.0 g and dissolve in sufficient *water* to produce 500.0 ml (solution A).

For sodium—Dilute a suitable volume of solution A with a sufficient volume of a solution of *strontium chloride* so that the final solution contains a 1500- to 2000-fold excess of strontium ions and determine by Method A for *atomic absorption spectrophotometry*, Appendix 5.16B, measuring at 589 nm and using *sodium solution FP*, suitably diluted with the strontium chloride solution, for the standard solutions or, alternatively by Method A for *flame photometry*, Appendix 5.16A. Each g of Sodium Chloride, of Sodium Bicarbonate and of Sodium Citrate is equivalent to 0.3934, 0.2737 and 0.2345 g of Na^+ respectively.

For potassium—Dilute a suitable volume of solution A with a sufficient volume of solution of *strontium chloride* so that the final solution contains a 1500- to 2000-fold excess of strontium ions and determine by Method A for *atomic absorption spectrophotometry*, Appendix 5.16B, measuring at 767 nm and using *potassium solution FP*, suitably diluted with the strontium chloride solution, for the standard solutions or, alternatively by Method A for *flame photometry*, Appendix 5.16A. Each g of Potassium Chloride is equivalent to 0.5245 g of K^+.

For total chloride—Titrate 50 ml of solution A with *0.1N silver nitrate*, using *potassium chromate solution* as indicator. Each ml of *0.1N silver nitrate* is equivalent to 0.003545 g of Cl^-. Each g of Sodium Chloride and of Potassium Chloride is equivalent to 0.6066 and 0.4756 g of Cl^- respectively.

For bicarbonate—Titrate 100 ml of solution A with *0.1N sulphuric acid*, using *methyl orange solution* as indicator. Each ml of *0.1N sulphuric acid* is equivalent to 0.006101 g of HCO_3^-. Each g of Sodium Bicarbonate is equivalent to 0.7263 g of HCO_3^-.

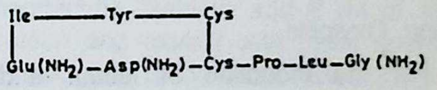
For citrate—Weigh accurately about 0.7 g and dissolve in 20 ml of *glacial acetic acid* by heating at about 50°. Cool and titrate with *0.1N perchloric acid*, using *1-naphtholbenzein solution* as indicator. Each ml of *0.1N perchloric acid* is equivalent to 0.006303 g of $C_6H_5O_7^{-3}$. Each g of Sodium Citrate is equivalent to 0.6430 g of $C_6H_5O_7^{-3}$.

For dextrose—Weigh accurately about 7.5 g, dissolve in 40 ml of *water*, add 0.5 ml of *dilute ammonia solution*, and dilute to 50 ml with *water*. Mix well, allow to stand for thirty minutes and measure the *optical rotation* in a 2-dm tube, Appendix 5.12. The observed rotation in degrees multiplied by 0.9477 and 1.0424 represents the weight in g of anhydrous dextrose and dextrose monohydrate respectively, as appropriate, in the weight taken for the **Assay.**

Storage: Store in air-tight containers in a dry place. Sachets, preferably made of aluminium foil, containing sufficient powder for a single dose or for a day's treatment are usually satisfactory to prevent ingress of moisture. Powders for use in hospitals may be presented in bulk containers containing sufficient quantity to produce a volume of solution appropriate to the daily requirements of the hospital concerned.

Labelling: The label on the container states (1) for preparations conforming to one of the three formulations described above, the appropriate title, viz. Oral Rehydration Salts-A or Oral Rehydration Salts-Bicarbonate or Oral Rehydration Salts-Citrate; (2) for sachets, the total weights, in grams, of the constituents; (3) for bulk containers, the weights, in grams, of the constituents in a stated quantity, in grams, of the ORS powder; (4) the total weight of contents of the container; (5) the directions for use; (6) that any portion of the solution prepared from the oral powder that remains unused 24 hours after preparation should be discarded; and (7) the storage conditions.

Oxytocin



$C_{43}H_{66}N_{12}O_{12}S_2$ Mol. Wt. 1007.23

Category: Oxytocic.

Dose: For the induction of labour and for the stimulation of uterine contractions during labour by slow intravenous infusion, 1 to 5 Units in 1 litre of 5 per cent Dextrose Injection.

For the control of post-partum haemorrhage, by subcutaneous, intramuscular, or slow intravenous injection, 2 to 5 Units.

Description: White or greyish-white powder.

Solubility: Soluble in *water*, in *n-butyl alcohol* and in *s-butyl alcohol*.

Standards: Oxytocin is a cyclic nonapeptide hormone containing the oxytocic principle obtained by a process of fractionation from the posterior lobe of the pituitary of healthy oxen or other mammals or by synthesis. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated potency.

Identification: It gives rise to an appropriate response when used as directed under *biological assay of oxytocin*, Appendix 2.12, at a concentration of not more than 0.01 Unit per ml of the bath fluid.

Vasopressor activity (for Oxytocin of natural origin): Not greater than 1 Unit (pressor) per 20 Units of oxytocic activity, when assayed by the *biological assay of vasopressin*, Appendix 2.13.

Assay: Carry out the *biological assay of oxytocin*, Appendix 2.12. The fiducial limits of error of the estimated potency are not less than 80 per cent and not more than 125 per cent of the stated potency.

Storage: Store in well-closed containers in a cool, dry place.

Labelling: The label on the container states (1) the potency as the number of Units (oxytocic) per mg; (2) the source of the preparation; (3) the date after which the contents are not intended to be used; and (4) the storage conditions.

Oxytocin Injection

Category: Oxytocic

Dose: For the induction of labour and for the stimulation of uterine contractions during labour, 1 to 5 Units in 1 litre of 5 per cent Dextrose Injection.

For the control of post-partum haemorrhage, by subcutaneous, intramuscular, or slow intravenous injection, 2 to 5 Units.

Usual strengths: 5 Units per ml; 10 Units per ml.

Description: Clear, colourless solution.

Standards: Oxytocin injection is a sterile solution of Oxytocin in Water for Injection. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated potency.

Identification: Complies with the **Identification** test described under Oxytocin.

pH: Between 2.5 and 4.5, Appendix 5.10.

Other requirements: Complies with the requirements stated under Injections.

Vasopressor activity and **Assay:** Complies with the requirements stated under Oxytocin.

Storage: Store at a temperature between 2° and 8°.

Labelling: The label on the container states (1) the potency as the number of Units (oxytocic) per ml; (2) either the animal source of the oxytocin or that it is synthetic; (3) the date after which the contents are not intended to be used; and (4) the storage conditions.

Oxytocin Nasal Solution

Category: Oxytocic.

Usual strength: 40 Units per ml.

Description: Clear, colourless solution.

Standards: Oxytocin Nasal Solution is a solution of Oxytocin in Purified Water. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated potency. It may contain suitable preservatives.

Identification: Complies with the **Identification** test described under Oxytocin.

pH: Between 3.7 and 4.3, Appendix 5.10.

Vasopressor activity and **Assay:** Complies with the requirements stated under Oxytocin.

Storage: Store at a temperature between 2° and 15°.

Labelling: The label on the container states (1) the potency as the number of Units (oxytocic) per ml; (2) either the animal source of oxytocin or that it is synthetic; (3) that the preparation is intended for intranasal administration only; (4) the date after which the contents are not intended to be used; and (5) the storage conditions.

Paracetamol Syrup

Category: Analgesic and antipyretic.

Dose: Paracetamol. Upto 0.5 g in accordance with the needs of the patient.

Usual strength: 125 mg per 5 ml.

Standards: Paracetamol Syrup is a solution containing Paracetamol in a suitable flavoured vehicle. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_8H_9NO_2$.

Identification: Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 65 volumes of *chloroform,* 25 volumes of *acetone*, 10 volumes of *toluene* and 0.5 volume of *glacial* *acetic acid* as the mobile phase. Apply separately to the plate 10 µ of each of the following two solutions. For solution (1) dilute 1.0 ml to 10.0 ml with *methyl alcohol* and filter, if necessary. Solution (2) is a 0.24 per cent w/v solution of *paracetamol R.S.* After removal of the plate, allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

pH: Between 3.8 and 6.1, Appendix 5.10.

4-Aminophenol: Carry out the method for *high performance liquid chromatography*, Appendix 5.4.4, using the following solutions. Solution (1) contains 0.0024 per cent w/v of *4-aminophenol* in the mobile phase. For solution (2) shake 5.0 ml of the syrup with 15 ml of the mobile phase, dilute to 25.0 ml with the mobile phase and filter if necessary.

Carry out the chromatographic procedure using (a) a stainless steel column (20 cm × 4.6 mm) packed with stationary phase L1, (b) *0.01M sodium butanesulphonate* in a mixture of 85 volumes of *water*, 15 volumes of *methyl alcohol* and 0.4 volume of *formic acid* as the mobile phase with a flow rate of 2.0 ml per minute and (c) a detection wavelength of 272 nm.

In the chromatogram obtained with solution (2) the area of any peak corresponding to 4-aminophenol is not greater than the area of the peak in the chromatgram obtained with solution (1). In the chromatogram obtained with solution (2) peaks with a long retention time may occur due to preservatives in the syrup.

Assay: Carry out the method for *high performance liquid chromatography*, Appendix 5.4.4, using the following solutions. Solution (1) contains 0.012 per cent w/v of *paracetamol R.S.* in the mobile phase. For solution (2) weigh accurately a quantity equivalent to about 24 mg of Paracetamol, mix with 100 ml of the mobile phase, add sufficient quantity of the mobile phase to produce 200.0 ml and filter, if necessary. Carry out the chromatographic procedure using the conditions described in the test for **4-aminophenol** but using a detection wavelength of 243 nm. Determine the weight per ml of the syrup and calculate the content of $C_8H_9NO_2$, weight in volume.

Storage: Store in tightly-closed, light-resistant containers.

Pheniramine Maleate Injection

Category: Antihistaminic.

Dose: Pheniramine Maleate, by intramuscular or slow intravenous injection, 25 to 50 mg daily, in divided doses.

Usual strength: 22.75 mg per ml.

Standards: Pheniramine Maleate Injection is a sterile solution of Pheniramine Maleate in Water for Injection. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Pheniramine Maleate, $C_{16}H_{20}N_2,C_4H_4O_4$.

Identification: (A) To a volume equivalent to 0.5 g of Pheniramine Maleate add 8 ml of *strong ammonia solution* and extract with three quantities, each of 5 ml, of *chloroform.* Evaporate the aqueous solution to dryness, add 0.2 ml of *dilute sulphuric acid* and 5 ml of *water* and extract with four quantities, each of 25 ml, of *solvent ether.* Dry in a current of warm air. The residue melts at about 132°, Appendix 5.11.

(B) To the residue obtained in **Identification** test (A) add 50 mg of *resorcinol* and 1 ml of *sulphuric acid.* heat in a water-bath for 2 minutes, shake well, heat for 30 minutes and cool in ice. Carefully add 5 ml of *water;* a yellow colour is produced. To 2 ml of the solution add 3 ml of 50 per cent w/v solution of *ammonium acetate,* previously cooled in ice; a pink colour is produced which persists for at least 10 minutes in the cooled solution.

(C) Evaporate the chloroform extract obtained in **Identification** test (A) on a water-bath. Add 35 ml of *picric acid solution,* saturated at 65°, and maintain at 65° for 2 minutes. Collect the precipitate, wash with a few small portions of *alcohol* and dry at 105° for one hour; the residue melts at about 200°, Appendix 5.11.

pH: Between 4.5 and 5.5., Appendix 5.10.

Other requirements: Complies with the requirements stated under Injections.

Assay: To an accurately measured volume equivalent to about 110 mg of Pheniramine Maleate add sufficient *water* to produce 50.0 ml and mix well. To 20.0 ml add sufficient *N sodium hydroxide* to make the solution just alkaline to *litmus paper,* add 2 ml in excess and extract with two quantities, each of 50 ml, of *solvent ether.* Wash each extract in succession with 20, 20 and 5 ml of *0.1N hydrochloric acid,* dilute the combined acid extracts to 100.0 ml with *0.1N hydrochloric acid* and mix. Dilute 5.0 ml to 100.0 ml with *0.1N hydrochloric acid* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 265 nm, Appendix 5.15A. Calculate the content of $C_{16}H_{20}N_2,C_4H_4O_4$ taking 210 as the value of E (1 per cent, 1-cm) at the maximum at about 265 nm.

Storage: Store in single-dose or multiple-dose, light-resistant containers.

Piperazine Citrate Syrup

Category: Anthelmintic.

Dose: *For threadworms*—Children: The equivalent of 40 mg of piperazine hydrate per kg of body weight daily, in divided doses. Adults: The equivalent of 1 to 2 g of piperazine hydrate daily, in divided doses.

For roundworms—Children: The equivalent of 120 mg of piperazine hydrate per kg of body weight to a maximum of 4 g, as a single dose. Adults: The equivalent of 4 g of piperazine hydrate, as a single dose.

Usual strength: The equivalent of 0.75 g of piperazine hydrate in 5 ml.

NOTE—100 mg of Piperazine Citrate is approximately equivalent to 80 mg of Piperazine Hydrate.

Standards: Piperazine Citrate Syrup contains a quantity of Piperazine Citrate equivalent to not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of piperazine hydrate, $C_4H_{10}N_2,6H_2O$.

Identification: (A) To 2 ml add 5 ml of *3N hydrochloric acid* and add with stirring 1 ml of a 50 per cent w/v solution of *sodium nitrite.* Chill in an ice-bath for 15 minutes, stirring if necessary to induce crystallisation. Filter the crystals through a sintered-glass funnel, wash with 10 ml of cold *water* and dry at 105°; the crystals melt between 156° and 160°, Appendix 5.11.

(B) Warm 10 ml with *decolorising charcoal,* add 10 ml of *water* and filter. The filtrate complies with the following tests:

(i) Boil 5 ml with an excess of *mercuric sulphate solution* and filter. Boil the filtrate with 0.25 ml of *potassium permanganate solution;* the permanganate solution is decolorised and a white precipitate is produced.

(ii) Acidify 5 ml with *2N sulphuric acid,* add 0.25 ml of *potassium permanganate solution,* warm until the colour of the permanganate is discharged. Add an excess of *bromine water;* a white precipitate is formed either immediately or on cooling.

Assay: Weigh accurately a quantity equivalent to about 0.2 g of piperazine hydrate, add 10 ml of *water,* 3.5 ml of *N sulphuric acid* and 100 ml of *picric acid solution.* Heat on a water-bath for one hour and filter through a sintered-glass filter (porosity 4 or equivalent). Wash the residue with successive quantities, each of a mixture of equal volumes of *water* and saturated solution of *picric acid,* until the washings are free from sulphate. Continue washing of the residue with five quantities, each of 10 ml, of *ethyl alcohol* and dry the residue to constant weight at 105°. Each g of the residue is equivalent to 0.3567 g of $C_4H_{10}N_2,6H_2O$. Determine the weight per ml of the syrup and calculate the content of piperazine hydrate in 5 ml of the syrup.

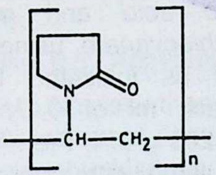
Storage: Store in tightly-closed, light-resistant containers in a cool place.

Labelling: The label on the container states the strength in terms of the equivalent amount of piperazine hydrate in 5 ml.

पुस्तकालय

Povidone

Polyvinylpyrrolidone; Polyvidone



$(C_6H_9NO)_n$

Category: Pharmaceutical aid (tablet binder, coating agent, dispersing and suspending agent).

Description: White to creamy-white powder; odourless or almost odourless; hygroscopic.

Solubility: Soluble in *water*, in *alcohol*, and in *chloroform*; practically insoluble in *solvent ether*.

Standards: Povidone is poly(2-oxypyrrolidin-1-yl ethylene). It consists of linear polymers of 1-vinyl-pyrrolidin-2-one. Its viscosity in aqueous solution, relative to that of water, expressed as K-value, varies from about 10 to 95. The K-value of Povidone having a declared value of 15 or less is not less than 85.0 per cent of the declared value. The K-value of Povidone having a declared value or declared value range with an average of more than 15 is not less than 90.0 per cent and not more than 108.0 per cent of the declared value or average of the declared value range. It contains not less than 11.5 per cent and not more than 12.8 per cent of nitrogen, N, calculated with reference to the anhydrous substance.

Identification: (A) To 0.5 ml of a 10 per cent w/v solution (solution A) add 5 ml of *water*, 10 ml of *N hydrochloric acid* and 2 ml of a 10 per cent w/v solution of *potassium dichromate* ; an orange-yellow precipitate is produced.

(B) To 1 ml of solution A add 0.2 ml of *dimethylaminobenzaldehyde reagent* and 0.1 ml of *sulphuric acid*; a pink colour is produced.

(C) To 2 ml of solution A add 5 ml of *water* and 0.2 ml of *iodine solution*; a deep red colour is produced.

Arsenic: Not more than 2 parts per million, Appendix 3.2.1.

Lead: Not more than 10 parts per million, determined on 1.0 g dissolved in 25 ml of *water*, Appendix 3.2.6.

Aldehydes: Not more than 0.2 per cent calculated as acetaldehyde, C_2H_4O, and determined by the following method. Boil 10.0 g in 100 ml of *9N sulphuric acid* under a reflux condenser for 45 minutes. Cool, fit a distillation head and distil until about 100 ml of distillate is collected in a flask placed-in an ice-bath and containing 20 ml of *N hydroxylamine hydrochloride*, previously adjusted to pH 3.1. Titrate the distillate with *0.1N sodium hydroxide* to a pH of 3.1. Perform a blank determination and make any necessary correction. Each ml of *0.1N sodium hydroxide* is equivalent to 0.004405 g of C_2H_4O.

Vinylpyrrolidinone: Not more than 0.2 per cent, determined by the following method. Dissolve 10.0 g in 80 ml of *water*, add 1 g of *sodium acetate* and titrate with *0.1N iodine* until a persistent colour is obtained. Add an additional 3.0 ml of *0.1N iodine*, allow to stand for ten minutes and titrate the excess iodine with *0.1N sodium thiosulphate*, using *starch solution*, added towards the end of the titration, as indicator. Perform a blank determination using the same total volume of *0.1N iodine*, accurately measured. The difference between the titrations represents the amount of iodine consumed by the vinylpyrrolidone monomer that may be present. Not more than 3.6 ml of *0.1N iodine* is consumed.

K-value: Weigh accurately a quantity of undried Povidone equivalent on the anhydrous basis to the amount specified as follows: For Povidone having a declared K-value of 18 or less, 5.0 g and for Povidone having a declared K-value of more than 18, 1.0 g. Dissolve in about 50 ml of *water* and mix. Allow to stand for one hour. Carry out Method B for the *determination of viscosity* at 25° ±0.2 °, using a size 1 suspended level viscometer, Appendix 5.18. Calculate the K-value from the expression:

$$\frac{\sqrt{300c \log z + (c + 1.5c \log z)^2} + 1.5\ c \log z - c}{0.15c + 0.003c^2}$$

in which c is the weight in g, on the anhydrous basis, of the substance being examined, in each 100.0 ml of solution, and z is the viscosity of the test solution relative to that of water.

Nitrogen content: Proceed as directed under *determination of nitrogen*, Method C, Appendix 3.3.5, using 0.3 g, accurately weighed, and 11 ml of *nitrogen-free sulphuric acid*. For complete destruction of organic matter repeat the addition of hydrogen peroxide (usually three to six times) until a clear, light-green solution is obtained, then heat for a further four hours.

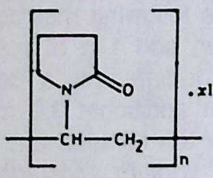
Sulphated ash: Not more than 0.1 per cent, Appendix 3.2.7.

Water: Not more than 5.0 per cent w/w, determined on 0.5 g, Appendix 3.3.25.

Storage: Store in tightly-closed containers.

Labelling: The label on the container states the viscosity in terms of a K-value or K-value range.

Povidone-Iodine



$(C_6H_9NO)_n.xI$

Category: Topical anti-infective; antiseptic.

Description: Yellowish-brown amorphous powder; odour, slight and characteristic.

Solubility: Soluble in *water* and in *alcohol*; practically insoluble in *chloroform*, in *acetone*, in *hexane* and in *solvent ether*.

Standards: Povidone-Iodine is a complex of Iodine with Povidone. It contains not less than 9.0 per cent and not more than 12.0 per cent of available iodine, I, calculated with reference to the dried substance.

Identification: (A) Add a drop of a 10 per cent w/v solution to a mixture of 1 ml of *starch solution* and 9 ml of *water*; a deep blue colour is produced.

(B) Spread 1 ml of a 10 per cent w/v solution over an area of about 20 cm × 20 cm on a glass plate, and allow to dry in air at room temperature and in an atmosphere of low humidity overnight; a brown, dry, non-smearing film is formed, and it dissolves readily in *water*.

Heavy metals: Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Nitrogen: Between 9.5 per cent and 11.5 per cent, calculated with reference to the dried substance and determined on about 0.3 g, accurately weighed, by Method A, Appendix 3.3.5.

Iodide: Not more than 6.6 per cent, calculated with reference to the dried substance and determined by the following method. Weigh accurately about 0.5 g and dissolve in 100 ml of *water*; add sufficient *sodium bisulphite solution* until the colour of iodine is discharged. Add 25.0 ml of *0.1N silver nitrate* and 10 ml of *nitric acid* and mix. Titrate with *0.1N ammonium thiocyanate*, using *ferric ammonium sulphate solution* as indicator. Perform a blank determination. Each ml of *0.1N silver nitrate* is equivalent to 0.01269 g of I. From the percentage of total iodine, calculated with reference to the dried substance, subtract the percentage of available iodine to obtain the percentage of iodide.

Sulphated ash: Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying: Not more than 8.0 per cent, determined on 5.0 g by drying in an oven at 105° until the difference between two successive weighings at one hour intervals is not more than 5.0 mg.

Available iodine: Weigh accurately about 5 g, transfer to a beaker and add 200 ml of *water*. Cover the beaker and stir with a mechanical stirrer at room temperature for not more than an hour to dissolve as completely as possible. Titrate immediately with *0.1N sodium thiosulphate*, using 3 ml of *starch solution*, added towards the end of the titration, as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N sodium thiosulphate* is equivalent to 0.01269 g of iodine, I.

Storage: Store in tightly-closed, light-resistant containers.

Povidone-Iodine Solution

Povidone-Iodine Topical Solution; Polyvidone-Iodine Solution

Category: Topical anti-infective; antiseptic.

Usual strengths: 5, 7.5 and 10 per cent w/v.

Description: Reddish-brown solution.

Standards: Povidone-Iodine Solution is a solution of Povidone-Iodine in Purified Water. It contains not less than 85.0 per cent and not more than 120.0 per cent of the stated amount of Iodine, I. It may contain a small amount of alcohol.

Identification: (A) Add 1 ml of a dilution containing about 0.05 per cent of iodine to a mixture of 1 ml of *starch solution* and 9 ml of *water;* a deep blue colour is produced.

(B) Transfer 10 ml to a 50-ml conical flask, avoiding contact with the neck of the flask. Cover the mouth of the flask with a small disc of filter paper and wet it with a drop of *starch solution;* no blue colour appears within 60 seconds.

pH: Not more than 6.5, Appendix 5.10.

Alcohol (*if present***):** Not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of C_2H_5OH, determined by Method I. Appendix 5.2A, after decolorising the sample with just sufficient quantity of a 10 per cent w/v solution of *sodium thiosulphate* and treating with a few drops of *dilute sodium hydroxide solution.*

Assay: To an accurately measured volume equivalent to about 50 mg of iodine add sufficient *water* to produce not less than 30 ml and titrate immediately with *0.02N sodium thiosulphate,* using 3 ml of *starch solution,* added towards the end of the titration, as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.02N sodium thiosulphate* is equivalent to 0.00253 g of Iodine, I.

Storage: Store in tightly-closed, light-resistant containers.

Labelling: The label on the container states the quantities of iodine and alcohol (if present) as percentages w/v.

Promethazine Syrup

Promethazine Hydrochloride Syrup

Category: Antihistaminic; anti-emetic.

Dose: Promethazine Hydrochloride. 20 to 50 mg daily, in single or divided doses.

Usual strength: 5 mg per 5 ml.

Standards: Promethazine Syrup contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{17}H_{20}N_2S,HCl$.

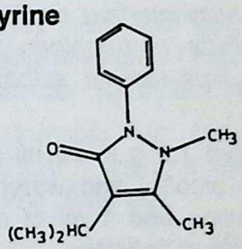
Identification: Complies with **Identification** test (B) described under Promethazine Hydrochloride. For solution (1) dilute a suitable volume of the syrup with *chloroform* to produce a solution containing 2 mg of Promethazine Hydrochloride per ml. Solution (2) is a 0.2 per cent w/v solution of *promethazine hydrochloride R.S.* in *chloroform.*

Assay: Carry out the following procedure protected from light. Weigh accurately a quantity equivalent to 20 mg of Promethazine Hydrochloride and add sufficient *water* to produce 100.0 ml. To 10.0 ml of this solution add 20 ml of *palladium chloride reagent* and sufficient *water* to produce 50.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 472 nm, Appendix 5.15A, using as blank a solution prepared by diluting 20 ml of *palladium chloride reagent* to 50.0 ml with *water.* Calculate the content of $C_{17}H_{20}N_2S,HCl$ taking 110 as the value of E (1 per cent, 1-cm) at the maximum at about 472 nm. Determine the weight per ml of the syrup and calculate the content of $C_{17}H_{20}N_2S,HCl$, weight in volume.

Storage: Store in tightly-closed, light-resistant containers in a cool place.

Propyphenazone

Isopropylantipyrine



$C_{14}H_{18}N_2O$ Mol. Wt. 230.31

Category: Analgesic, antipyretic and anti-inflammatory.

Dose: 1.5 to 3 g daily, in divided doses.

Description: White crystalline powder; odourless; taste, slightly bitter.

Solubility: Slightly soluble in *water*; soluble in *solvent ether*; freely soluble in *alcohol,* in *chloroform* and in *benzene.*

Standards: Propyphenazone is 1,2-dihydro-1,5-dimethyl-4-(1-methylethyl)-2-phenyl-3H-pyrazol-3-one. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{14}H_{18}N_2O$, calculated with reference to the dried substance.

Identification: (A) Dissolve 0.2 g in sufficient *water* to produce 100 ml (solution A). To 2 ml add 3 drops of *tannic acid solution;* a white precipitate is produced.

(B) To 2 ml of solution A add 1 drop of *ferric chloride test solution;* a red colour is produced which, on addition of 3 drops of *sulphuric acid,* turns pale yellow.

(C) Add 5 ml of solution A to a mixture of 5 ml of *potassium ferricyanide solution* and 2 drops of *ferric chloride test solution*; a dark green colour develops gradually.

Melting range: Between 103° and 105°, Appendix 5.11.

Arsenic: Not more than 10 parts per million. Appendix 3.2.1.

Heavy metals: Not more than 20 parts per million, determined by Method A on a solution prepared by dissolving 1.0 g in 25 ml of *acetone*, adding 2 ml of *dilute acetic acid* and diluting to 50 ml with *water*, Appendix 3.2.4.

Chloride: 0.4 g dissolved in 30 ml of a mixture of equal volumes of *alcohol* and *water* to which 6 ml of *dilute nitric acid* is added complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate: 0.3 g dissolved in 30 ml of a mixture of equal volumes of *sulphate-free alcohol* and *water* to which 2 ml of *dilute hydrochloric acid* is added complies with the *limit test for sulphates*, Appendix 3.2.8.

Antipyrine: Dissolve 1.0 g in 10 ml of a mixture of equal volumes of *alcohol* and *water*, add 1 ml of *sodium nitrite solution* and 1 ml of *dilute sulphuric acid;* no green colour develops.

Sulphated ash: Not more than 0.1 per cent. Appendix 3.2.7.

Loss on drying: Not more than 0.5 per cent, determined on 1.0 g by drying 'in vacuo' for 5 hours, Appendix 5.8.

Assay: Weigh accurately about 0.4 g of the dried material, dissolve in 60 ml of *glacial acetic acid* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02303 g of $C_{14}H_{18}N_2O$.

Storage: Store in tightly-closed containers.

Protamine Sulphate

Category: Heparin antagonist.

Dose: By slow intravenous injection, in accordance with the needs of the patient, upto 50 mg or as determined by the physician.

Description: White or almost white powder; hygroscopic.

Solubility: Sparingly soluble in *water;* practically insoluble in *alcohol*, in *chloroform* and in *solvent ether.*

Standards: Protamine Sulphate is a purified mixture of the sulphates of basic peptides prepared from the sperm or mature testes of suitable species of fish which has the property of neutralising heparin. Each mg of Protamine Sulphate neutralises not less than 100 Units of heparin activity, calculated with reference to the dried substance. It is prepared in conditions designed to minimise microbial contamination.

Identification: (A) Heat 2 ml of a 2 per cent w/v solution in a water-bath at 60° and add 0.1 ml of *mercuric sulphate solution;* no precipitate is produced. Cool the mixture in ice; a precipitate is produced.

(B) To 0.5 ml of a 2 per cent w/v solution add 4.5 ml of *water*, 1.0 ml of a 10 per cent w/v solution of *sodium hydroxide* and 1.0 ml of a 0.02 per cent w/v solution of *1-naphthol* and mix. Cool to 5° and add 0.5 ml of *alkaline sodium hypobromite solution.* An intense red colour is produced.

(C) A solution (1 in 50) gives the reactions of *sulphates*, Appendix 3.1.

Specific optical rotation: Between −65° and −85°, determined at 20° in a 1 per cent w/v solution in *0.1N hydrochloric acid*, Appendix 5.12.

Light absorption: Dissolve 0.20 g in sufficient *water* to produce 10.0 ml. Dilute 2.5 ml to 5.0 ml with *water.* The *extinction* of a 1-cm layer of the resulting solution at 260 to 280 nm is not more than 0.5, Appendix 5.15A.

Heavy metals: Not more than 20 parts per million, determined on 1.0 g, by Method B. Appendix 3.2.4.

Mercury: Not more than 10 parts per million when determined by the following method. Add 20 ml of a mixture of equal volumes of *nitric acid* and *sulphuric acid* to 2 g in a 250-ml flask fitted with a ground-glass stopper, boil under a reflux condenser for 1 hour, cool and carefully dilute with *water.* Boil until nitrous fumes are no longer evolved. Cool, carefully dilute the solution to 200 ml with *water*, mix and filter. Transfer 50 ml of the filtrate to a separating funnel. Shake with successive small quantities of *chloroform*

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until the chloroform layer remains colourless. To the aqueous layer add 25 ml of *2N sulphuric acid,* 115 ml of *water* and 10 ml of a 20 per cent w/v solution of *hydroxylamine hydrochloride.* Titrate with *dithizone solution;* after each addition, shake the mixture 20 times and towards the end-point of the titration allow to separate and discard the chloroform layer. Titrate until bluish-green colour is produced. Calculate the content of mercury using the equivalent of mercury in µg per ml of titrant determined in the standarisation of dithizone solution.

Iron: A 10.0 per cent w/v solution in *water* complies with the *limit test for iron,* Appendix 3.2.5.

Nitrogen: Between 21.0 per cent and 26.0 per cent, calculated with reference to the dried substance and determined by Method C, Appendix 3.3.5.

Sulphate: Between 16 per cent and 24 per cent, determined by the following method. Weigh accurately about 0.15 g and dissolve in 15 ml of *water* in a beaker. Add 5 ml of *2N hydrochloric acid* and heat to boiling. Add slowly to the boiling solution 10 ml of *barium chloride solution.* Cover the beaker and heat on a water-bath for one hour. Filter and wash the precipitate several times with small quantities of hot *water.* Dry and ignite the residue to constant weight at 600°. Each g of residue is equivalent to 0.4117 g of sulphate, SO_4.

Loss on drying: Not more than 5.0 per cent, determined on 1.0 g by drying in an oven at 105° for 3 hours, Appendix 5.8.

Assay: Carry out the *assay of protamine sulphate,* Appendix 2.43.

Protamine Sulphate intended for the manufacture of parenteral preparations complies with the following additional requirements.

Pyrogens: Complies with the *test for pyrogens,* Appendix 2.36, using 1 ml of a solution containing 10 mg per ml per kg of the rabbit's weight.

Undue toxicity: Complies with the test described under Bacitracin using 0.5 ml of a solution containing 0.5 mg dissolved in *water for injection.*

Storage: Store in tightly-closed containers in a cold place. If it is intended for use in the manufacture of parenteral preparations, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling: The label on the container states (1) whether or not the contents are intended for use in the manufacture of parenteral preparations; (2) the date after which the contents are not intended to be used; and (3) the storage conditions.

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Protamine Sulphate Injection

Category: Heparin antagonist.

Dose: Protamine Sulphate. By slow intravenous injection, in accordance with the needs of the patient, upto 50 mg or as determined by the physician.

Usual strengths: 50 mg in 5 ml; 100 mg in 10 ml.

Standards: Protamine Sulphate Injection is a sterile solution of Protamine Sulphate in Water for Injection. It contains not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of Protamine Sulphate.

pH: Between 2.5 and 3.5, Appendix 5.10.

Pyrogens: Complies with the *test for pyrogens,* Appendix 2.36, using a volume containing 10 mg of Protamine Sulphate per kg of the rabbit's weight.

Undue toxicity: Complies with the *test for undue toxicity,* Appendix 2.37.1. using a volume containing 0.5 mg of Protamine Sulphate.

Other requirements: Complies with the requirements stated under Injections.

Assay: Carry out the *assay of protamine sulphate,* Appendix 2.42.

Storage: Store in single-dose containers in cold place.

Labelling: The label on the container states (1) that the dose is calculated from the results of determinations of the amount required to produce an acceptable blood-clotting time in the patient; and (2) the approximate number of units of heparin activity each ml is capable of neutralising.

Pyrimethamine and Sulphadoxine Tablets

पुस्तकालय
गुरुकुल कांगड़ी विश्वविद्यालय

Category: Antiprotozoal.

Dose: Pyrimethamine, 25 to 50 mg and Sulphadoxine, 500 mg to 1 g, daily.

Usual strength: 25 mg of Pyrimethamine and 500 mg of Sulphadoxine.

Standards: Pyrimethamine and Sulphadoxine

Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amounts of Pyrimethamine, $C_{12}H_{13}ClN_4$, and Sulphadoxine, $C_{12}H_{14}N_4O_4S$.

Identification: Carry out the method for *thin-layer chromatography,* Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 4 volumes of *chloroform,* 4 volumes of *heptane,* 1 volume of *glacial acetic acid* and 4 volumes of a mixture of 1 volume of *methyl alcohol* and 19 volumes of *ethyl alcohol* as the mobile phase. Apply separately to the plate 10 μl of each of the following solutions. For solution (1) shake a quantity of the powdered tablets equivalent to 25 mg of Pyrimethamine with 50 ml of a 2 per cent v/v solution of *strong ammonia solution* in *methyl alcohol* for about 30 minutes and filter; solution (2) is a 0.05 per cent w/v solution of *pyrimethamine R.S.* in *methyl alcohol;* solution (3) is a 1.0 per cent w/v solution of *sulphadoxine R.S.* in *methyl alcohol.* After removal of the plate, allow it to dry in air, and examine under an ultra-violet lamp having a maximum output at about 254 nm. One of the principal spots in the chromatogram obtained with solution (1) corresponds to the spot in the chromatogram obtained with solution (2) and the other corresponds to the spot in the chromatogram obtained with solution (3).

Other requirements: Comply with the requirements stated under Tablets.

Assay: Prepare a solution containing 0.1 g of *phenacetin* (internal standard) in 100 ml of *acetonitrile* (solution A). Carry out the method for *high performance liquid chromatography,* Appendix 5.4.4, using the following solutions. For solution (1) weigh accurately a quantity of the powdered tablets equivalent to about 25 mg of Pyrimethamine and 500 mg of Sulphadoxine and shake with 35 ml of *acetonitrile* for 30 minutes in a 100-ml volumetric flask. Dilute to volume with the mobile phase consisting of a mixture of 4 volumes of a 1 per cent v/v solution of *glacial acetic acid* and I volume of *acetonitrile*, mix and filter. To 25.0 ml of the filtrate add 2.0 ml of solution A and sufficient volume of the mobile phase to produce 50.0 ml. For solution (2) weigh accurately about 25 mg of *pyrimethamine R.S.* and 500 mg of *sulphadoxine R.S.*, add 35 ml of *acetonitrile* and sufficient volume of the mobile phase to produce 100.0 ml and mix. To 25.0 ml add 2.0 ml of solution A and add sufficient volume of the mobile phase to produce 50.0 ml; mix well.

Carry out the chromatographic procedure using (a) a stainless steel column (30 cm × 4 mm) packed with stationary phase L1. (b) a mixture of 4 volumes of a 1 per cent v/v solution of *glacial acetic acid* and 1 volume of *acetonitrile* as the mobile phase with a flow rate of 2.0 ml per minute and (c) a detection wavelength of 254 nm. The relative retention times should be about 1.3 for pyrimethamine, 1.0 for phenacetin and 0.7 for sulphadoxine. Calculate the content of $C_{12}H_{13}ClN_4$ from the declared content of $C_{12}H_{13}ClN_4$ in the *pyrimethamine R.S.* and the content of $C_{12}H_{14}N_4O_4S$ from the declared content of $C_{12}H_{14}N_4O_4S$ in the *sulphadoxine R.S.*

Strorage: Store in well-closed, light-resistant containers.

Salbutamol Syrup

Category: Adrenergic (bronochodilator).

Dose: The equivalent of 6 to 16 mg of salbutamol daily, in divided doses.

Usual strength: The equivalent of 2 mg of salbutamol in 5 ml.

Standards: Salbutamol Syrup contains a quantity of Salbutamol Sulphate equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Salbutamol, $C_{13}H_{21}NO_3$.

Identification: (A) To 5 ml add 50 ml of a 2 per cent w/v solution of *borax,* 1 ml of a 3 per cent w/v solution of *aminopyrazolone* ,10 ml of a 2 per cent w/v solution of *potassium ferricyanide,* 10 ml of *chloroform,* shake and allow to separate; an orange-red colour develops in the chloroform layer.

(B) To 5 ml add sufficient *N sodium hydroxide* to make the solution alkaline, add 1 ml of *alkaline borate buffer pH 9.2* and 1 ml of a 0.04 per cent w/v solution of *2,6-dichloroquinone chlorimide* in *isopropyl alcohol;* a blue colour develops.

pH: Between 3.4 and 4.5, Appendix 5.10.

Assay: To an accurately measured volume equivalent to 4 mg of salbutamol add 25 ml of *0.1N sulphuric acid* and extract with two quantities, each of 50 ml, of *solvent ether.* Discard the ether extracts and dilute the aqueous solution with sufficient *water* to produce 250.0 ml. To 10 ml of this solution add sufficient *water* to produce 80 ml followed by 4 ml of a 5 per cent w/v solution of *sodium bicarbonate,* 4 ml of a 0.1 per cent w/v solution of *N,N-dimethyl-p-*

phenylenediamine dihydrochloride and 4 ml of a freshly-prepared 8 per cent w/v solution of *potassium ferricyanide.* Mix, allow to stand for 15 minutes protected from light and extract with two quantities, each of 10 ml, of *chloroform.* Filter the extracts through a plug of cotton and dilute with sufficient *chloroform* to produce 25.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 605 nm, Appendix 5.15A, using as the blank a solution prepared in a similar manner but omitting the substance being examined. Calculate the content of $C_{13}H_{21}NO_3$ from the *extinction* obtained by repeating the **assay** using *salbutamol sulphate R.S.* and from the declared content of $C_{13}H_{21}NO_3$ in the *salbutamol sulphate R.S.*

Storage: Store in tightly-closed, light-resistant containers in a cool place.

Labelling: The label on the container states the strength in terms of the equivalent amount of salbutamol in a suitable dose-volume.

Colloidal Silicon Dioxide

Colloidal Anhydrous Silica

SiO_2 Mol. Wt. 60.08

Category: Pharmaceutical aid (tablet excipient).

Description: Light, fine, white amorphous powder; odourless. It has a particle size of about 15 μm.

Solubility: Practically insoluble in *water* and in mineral acids with the exception of *hydrofluoric acid.* Dissolves in hot solutions of alkali hydroxides. 1 g shaken vigorously with 20 ml of *carbon tetrachloride* for 3 minutes produces a transparent gel.

Standards: Colloidal Silicon Dioxide is a submicroscopic, fumed silica prepared by the vapour-phase hydrolysis of a silicon compound. It contains not less than 99.0 per cent and not more than 100.5 per cent of SiO_2, calculated with reference to the ignited substance.

Identification: (A) Transfer about 5 mg to a platinum crucible and mix with about 20 mg of *anhydrous potassium carbonate.* Ignite at red heat over a burner for about ten minutes and cool. Dissolve the melt in 2 ml of *water,* warming if necessary, and slowly add 2 ml of *ammonium molybdate solution;* a deep yellow colour is produced.

(B) Place one drop of the yellow solution obtained in Identification test (A) on a filter paper and evaporate the solvent. Add one drop of a saturated solution of *o-tolidine* in *glacial acetic acid* and place the paper over *strong ammonia solution;* a greenish-blue spot is produced.

CAUTION—This test should be carried out in a well-ventilated hood and contact with o-tolidine should be avoided.

pH: Between 3.5 and 4.4, determined in a suspension of 1 g in 30 ml of *carbon dioxide-free water,* Appendix 5.10.

Chloride: To 1.4 g add a mixture of 20 ml of *2N nitric acid* and 20 ml of *water,* heat on a water-bath for 15 minutes, shaking frequently, filter and cool. The filtrate complies with the *limit test for chlorides,* Appendix 3.2.2.

Arsenic: Not more than 8 parts per million, Appendix 3.2.1.

Heavy metals: Not more than 25 parts per million. determined by Method A, Appendix 3.2.4, on 20 ml of a solution prepared in the following manner. Suspend 2.0 g in sufficient *water* to produce a semi-fluid slurry and dry at 140°. Filter the supernatant liquid through a membrane filter. To the residue in the centrifuge tube add 3 ml of *2N hydrochloric acid* and 9 ml of *water,* boil, centrifuge for 20 minutes and filter the supernatant liquid through the same membrane filter. Wash the residue with small quantities of water, combine the filtrates and washings and dilute to 50 ml with *water.* To 20 ml of the solution add 50 mg of *ascorbic acid* and 1 ml of *strong ammonia solution,* neutralise with *2N ammonia* and dilute to 25 ml with with *water.*

Loss on ignition: Not more than 2.0 per cent, determined on 0.2 g, accurately weighed, and by ignition at 1000° for 2 hours in a platinum crucible. The residue should be cooled in a desiccator before weighing.

Assay: To the residue obtained in the test for **Loss on ignition** add 0.2 ml of *sulphuric acid* and sufficient *alcohol* to moisten the residue completely.

add 6 ml of *hydrofluoric acid* and evaporate to dryness on a hot plate at 95° to 105°, avoiding loss from spurting. Wash the sides of the dish with 6 ml of *hydrofluoric acid,* evaporate to dryness in a well-ventilated hood, ignite at 1000°, allow to cool in a desiccator and weigh. The difference between the weight of the final residue and that of the residue obtained in the test for **Loss on ignition** represents the amount of SiO_2 in the amount of the substance taken for the test for loss on ignition.

Storage: Store in well-closed containers.

Sodium Alginate

Sodium Polymannuronate

Category: Pharmaceutical aid (viscosity increasing agent).

Description: Cream-coloured, coarse or fine powder; almost odourless and tasteless

Solubility: Soluble in *water,* forming a viscous, colloidal solution; insoluble in *alcohol,* in *chloroform,* in *solvent ether* and in aqueous acid solutions when the pH is below 3.

Standards: Sodium Alginate is the purified carbohydrate product extracted with dilute alkali from brown seaweeds *(Phaeophyceae).* It consists mainly of the sodium salt of alginic acid, a polyuronic acid composed of ß-D-mannuronic acid linked so that the carboxyl group of each unit is free while the aldehyde group is shielded by a glycosidic linkage.

Identification: (A) To 5 ml of a 1 per cent w/v solution add 1 ml of *calcium chloride solution;* a bulky, gelatinous precipitate is formed immediately.

(B) To 10 ml of the solution obtained in test (A) add 1 ml of *4N sulphuric acid;* a heavy, gelatinous precipitate is formed.

(C) The residue obtained in the test for **Ash** gives the reactions of *sodium,* Appendix 3.1.

Arsenic: Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals: Not more than 40 parts per million, determined on 0.5 g by Method B and using *nitric acid Sp* in place of *sulphuric acid Sp* to wet the sample, Appendix 3.2.4.

Microbial limits: 1 g meets the requirements of the test for the absence of *E.coli* and 10 g is free from *salmonellae, Appendix 4.5.*

Ash: Between 18.0 per cent and 24.0 per cent, determined on 2.0 g by Method II and igniting at a temperature of 800° ± 25°, Appendix 3.22.

Loss on drying: Not more than 15.0 per cent determined on 1.0 g by drying in an oven at 105° for 4 hours, Appendix 5.8.

Storage: Store in tightly-closed containers.

Sodium Formaldehyde Sulphoxylate

$HOCH_2SO_2Na,2H_2O$

CH_3NaO_3S Mol. Wt. 118.08

Category: Pharmaceutical aid (antioxidant).

Description: White crystals or hard white masses; odour, characteristic and garlic-like.

Solubility: Freely soluble in *water;* slightly soluble in *alcohol,* in *chloroform,* in *solvent ether* and in *benzene.*

Standards: Sodium Formaldehyde Sulphoxylate is monosodium hydroxymethane sulphinate. It contains an amount of CH_3NaO_3S equivalent to not less than 45.0 per cent and not more than 55.0 per cent of SO_2, calculated with reference to the dried substance. It may contain a suitable stabiliser such as sodium carbonate.

Identification: (A) Dissolve about 4 g in 10 ml of *water* in a test-tube and add 1 ml of *ammoniacal silver nitrate solution;* metallic silver is produced, either as a finely divided grey precipitate or as a bright metallic mirror on the inner surface of the tube.

(B) Add about 50 mg to a solution of 40 mg of *salicylic acid* in 5 ml of *sulphuric acid* and warm very gently; a permanent deep red colour develops.

Clarity and colour of solution: Dissolve 1 g in 20 ml of *water* and transfer 10 ml to a test-tube (20 mm × 150 mm); compare the solution with 10 ml of *water* in a similar test-tube. The liquids are equally clear and when viewed transversely by transmitted light exhibit no apparent difference in colour.

Alkalinity: Dissolve 1 g in 50 ml of *water*, add a few drops of *phenolphthalein solution* and titrate with *0.1N sulphuric acid;* not more than 3.5 ml is required for neutralisation.

pH: Between 9.5 and 10.5, determined in a 2.0 per cent w/v solution in *carbon dioxide-free water*, Appendix 5.10.

Iron: Not more than 10 parts per million, determined by the following method. Weigh accurately 1 g and carefully ignite, initially at a low temperature until thoroughly charred and finally at 500° to 600°, preferably in a muffle furnace, until all the carbon has burnt off. Cool, dissolve the residue in 2 ml of *hydrochloric acid* and dilute to 50 ml with *water.* Add about 50 mg of *ammonium persulphate* and 5 ml of *ammonium thiocyanate solution*, mix and transfer to a *Nessler cylinder.* The red colour of the solution is not deeper than that of 2.0 ml of a solution of iron prepared by dissolving 43.2 mg of *ferric ammonium sulphate* in 10 ml of *2N sulphuric acid* and sufficient *water* to produce 1000.0 ml and treated in the same manner.

Sulphide: Dissolve 6 g in 14 ml of *water* in a test-tube and wet a strip of *lead acetate paper* in the clear solution; no discolouration is evident within 5 minutes.

Sodium sulphite: Not more than 5.0 per cent calculated as Na_2SO_3 with reference to the dried substance and determined by the following method. Transfer 4.0 ml of the solution prepared for the **Assay** to a flask, add 2 ml of *formaldehyde solution* and titrate with the same *0.1N iodine* that is used for the **Assay,** adding *starch solution* towards the end of the titration. Calculate the percentage of Na_2SO_3 from the expression $78.775(V_2-V_1)/W$, in which V_1 and V_2 are the volumes in ml of *0.1N iodine* consumed in this test and in the **Assay** respectively and W is the weight in g of the sample taken for the **Assay.**

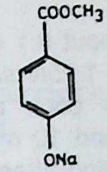
Loss on drying: Not more than 27 per cent, determined on 1.0 g by drying in an oven at 105° for three hours, Appendix 5.8.

Assay: Weigh accurately about 1 g, dissolve in about 25 ml of *water*, add sufficient *water* to produce 50.0 ml and mix. To 4.0 ml of the solution add 100 ml of *water* and titrate with *0.1N iodine*, using 3 ml of *starch solution*, added towards the end of the titration, as indicator. Each ml of *0.1N iodine* is equivalent to 0.001602 g of SO_2.

Storage: Store in well-closed, light-resistant containers in a cool place.

Sodium Methylparaben

Sodium Methyl Hydroxybenzoate



$C_8H_7NaO_3$ Mol. Wt. 174.13

Category: Pharmaceutical aid (antimicrobial preservative).

Description: White, crystalline powder; almost odourless; hygroscopic.

Solubility: Freely soluble in *water;* soluble in *alcohol;* practically insoluble in fixed oils.

Standards: Sodium Methylparaben is the sodium salt of methyl 4-hydroxybenzoate. It contains not less than 99.0 per cent and not more than the equivalent of 102.0 per cent of $C_8H_7NaO_3$, calculated with reference to the anhydrous substance.

Identification: (A) Dissolve 0.5 g in 5 ml of *water* and acidify to *litmus paper* with *hydrochloric acid;* a white precipitate is formed which after washing with *water* and drying, melts at about 126°, Appendix 5.11.

(B) Boil 10 mg of the precipitate obtained in test A with 10 ml of *water*, cool and add 0.05 ml of *ferric chloride solution;* a reddish-violet colour is produced.

(C) Dissolve 0.1 g of the precipitate obtained in test (A) in 2 ml of *alcohol*, boil and add 0.5 ml of *mercury nitrate solution;* a precipitate is formed and the supernatant liquid becomes red.

(D) Ignite a small quantity. The residue gives the reactions of *sodium*, Appendix 3.1.

Clarity of solution: Dissolve 1 g in 10 ml of *water;* the solution is clear.

pH: Between 9.5 and 10.5, determined in a 0.1 per cent w/v solution, Appendix 5.10.

Chloride: Dissolve 2.0 g in 100 ml of *water*, add 1 ml of *nitric acid* and filter. To 50 ml of the filtrate add 0.5 ml of *nitric acid* and 1 ml of *N silver nitrate;* the opalescence produced is not greater than the *standard opalescence* in the *limit test for chlorides,* Appendix 3.2.2.

Sulphate: 25 ml of the filtrate obtained in the test for **Chloride** complies with the *limit test for sulphates,* Appendix 3.2.8.

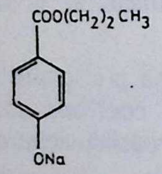
Water: Not more than 5.0 per cent w/w, Appendix 3.3.25.

Assay: Weigh acurately about 0.1 g and boil gently under reflux with 25 ml of *1.25N sodium hydroxide* for 30 minutes. Allow to cool, add immediately 50.0 ml of *0.1N bromine* and 10 ml of *hydrochloric acid.* Shake repeatedly during fifteen minutes, allow to stand for fifteen minutes, add 30 ml of *potassium iodide solution* and titrate the liberated iodine with *0.1N sodium thiosulphate,* using *starch solution* as indicator. Repeat the operaton with the same quantities of the same reagents in the same manner, omitting the substance being examined. The difference between the titrations represents the amount of bromine required by sodium methylparaben. Each ml of *0.1N bromine* is equivalent to 0.002902 g of $C_8H_7NaO_3$.

Storage: Store in tightly-closed containers.

Sodium Propylparaben

Sodium Propyl Hydroxybenzoate



$C_{10}H_{11}NaO_3$ Mol. Wt. 202.18

Category: Pharmaceutical aid (antimicrobial preservative).

Description: White, crystalline powder; odourless; hygroscopic.

Solubility: Freely soluble in *water;* soluble in *alcohol:* practically insoluble in fixed oils.

Standards: Sodium Propylparaben is the sodium salt of propyl 4-hydroxybenzoate. It contains not less than 99.0 per cent and not more than the equivalent of 102.0 per cent of $C_{10}H_{11}NaO_3$, calculated with reference to the anhydrous substance.

Identification: (A) Dissolve 0.5 g in 5 ml of *water* and acidify to *litmus paper* with *hydrochloric acid*; a white precipitate is formed which after washing with *water* and drying melts at about 95°, Appendix 5.11.

(B) Complies with **Identification** tests (B), (C) and (D) described under Sodium Methylparaben.

Clarity of solution, pH, Chloride, Sulphate and **Water:** Complies with the requirements stated under Sodium Methylparaben.

Assay: Carry out the **Assay** described under Sodium Methylparaben. Each ml of *0.1N bromine* is equivalent to 0.00337 g of $C_{10}H_{11}NaO_3$.

Storage: Store in tightly-closed containers.

Sodium Starch Glycollate

Sodium Carboxymethyl Starch

Category: Pharmaceutical aid (tablet disintegrant).

Description: Very fine, white or off-white, free-flowing powder; odourless or almost odourless.

Solubility: Practically insoluble in *water*; insoluble in most organic solvents.

Standards: Sodium Starch Glycollate is the sodium salt of a poly-$\propto$-glucopyranose in which some of the hydroxyl groups are in the form of carboxymethyl ether. It contains not less than 2.8 per cent and not more than 4.5 per cent of sodium, Na, calculated with reference to the dried substance.

Identification: (A) To a 2 per cent dispersion in *water* add one drop of *0.01 N iodine*; a dark blue colour is produced.

(B) The solution obtained in the test for **Heavy metals** gives the reactions of *sodium,* Appendix 3.1.

pH: Between 5.5 and 7.5, determined in a 2.0 per cent w/v dispersion in *carbon dioxide-free water,* Appendix 5.10.

Heavy metals: Not more than 20 parts per million, determined by Method A, Appendix 3.2.4, on 25 ml of a solution prepared in the following manner. To 4.0 g in a silica or platinum dish add 2 ml of a 50 per cent w/v solution of *sulphuric acid* and heat in a water-bath and then cautiously over a flame to about 600°. Continue heating until all black particles have disappeared, allow to cool, add 0.1 ml of *2N* *sulphuric acid*, heat to ignition once again and allow to cool. Add 0.1 ml of *2N ammonium carbonate*, evaporate to dryness and cautiously ignite. To the residue add 5 ml of *hydrochloric acid*, evaporate to dryness on a water-bath and dissolve the residue in 100 ml of *water*.

Iron: 50 ml of the solution obtained in the test for **Heavy metals** complies with the *limit test for iron*, Appendix 3.2.5.

Sodium chloride: Not more than 10.0 per cent, determined by the following method. Weigh accurately about 1 g, add 20.0 ml of *0.1N silver nitrate* and 30 ml of *nitric acid* and boil carefully for 30 minutes. Cool and add sufficient volume of a saturated solution of *potassium permanganate* to change the colour of the solution to pink. Discharge the colour by the dropwise addition of *hydrogen peroxide solution*, add 3 ml of *dibutyl phthalate* and titrate with *0.1N ammonium thiocyanate*, using *ferric ammonium sulphate solution* as indicator, shaking vigorously after each addition of the titrant. Each ml of *0.1N silver nitrate* is equivalent to 0.005844 g of NaCl.

Microbial limits: 1 g meets the requirements of the test for absence of *E. coli* and *salmonellae*, Appendix 4.5.

Loss on drying: Not more than 10.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay: Weigh accurately about 4 g and add 350 ml of a mixture of 4 volumes of *alcohol* and 1 volume of *water*, add 0.25 ml of *phenolphthalein solution* and mix. Add *N sodium hydroxide* dropwise until the colour of the suspension becomes faintly pink, shake for 30 minutes and decant through a sintered glass crucible. Repeat the extraction three times or more until the filtrate is free from chloride. Transfer the bulk of the residue to the crucible, wash the residue with small quantities of *alcohol* and dry it at 110° to constant weight. Weigh accurately about 0.5 g of the dried substance, add 80 ml of *glacial acetic acid*, heat under reflux for 2 hours, cool and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Each ml of *0.1N perchloric acid* is equivalent to 0.0023 g of Na.

Storage: Store in tightly-closed containers in a cool, dry place.

Sorbic Acid

$$CH_3CH{=}CHCH{=}CHCOOH$$

$C_6H_8O_2$ Mol. Wt. 112.13

Category: Pharmaceutical aid (antifungal and antibacterial agent).

Description: White or creamy-white, crystalline powder; odour, faint and characteristic.

Solubility: Slightly soluble in *water;* soluble in *alcohol* and in *solvent ether.*

Standards: Sorbic Acid is 2,4-hexadienoic acid. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_6H_8O_2$, calculated with reference to the anhydrous substance.

Identification: (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.00025 per cent w/v solution in *isopropyl alcohol* exhibits a maximum only at about 264 nm; *extinction* at about 264 nm, about 0.6, Appendix 5.15A.

(B) Dissolve 0.2 g in 2 ml of *alcohol* and add a few drops of *bromine solution;* the colour is discharged.

Melting range: Between 133° and 137°, Appendix 5.11.

Arsenic: Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals: Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Aldehyde: Not more than 0.15 per cent w/w, calculated as acetaldehyde, C_2H_4O and determined in the following manner. Dissolve 1.0 g in a mixture of 50 ml of *isopropyl alcohol* and 30 ml of *water,* adjust the pH to 4.0 with *N hydrochloric acid* and dilute to 100.0 ml with *water.* To 10.0 ml of the resulting solution add 1 ml of *decolorised magenta solution* and allow to stand for 30 minutes. The colour produced is not more intense than that produced by adding 1 ml of *decolorised* *magenta solution* to a mixture of 1.5 ml of a 0.010 per cent w/w solution of *acetaldehyde,* 4 ml of *isopropyl alcohol* and 4.5 ml of *water.*

Sulphated ash: Not more than 0.2 per cent, Appendix 3.2.7.

Water: Not more than 0.5 per cent w/w, Appendix 3.3.25.

Assay: Weigh accurately about 1.5 g and dissolve in 25 ml of *alcohol,* previously neutralised to *phenolphthalein solution* with *0.1N sodium hydroxide;* titrate with *N sodium hydroxide* using *phenolphthalein solution* as indicator. Each ml of *N sodium hydroxide* is equivalent to 0.1121 g of $C_6H_8O_2$.

Storage: Store in tightly-closed, light-resistant containers, in a cool place.

Stearyl Alcohol

Octadecyl Alcohol; 1-Octadecanol

Category: Pharmaceutical aid (stiffening agent).

Description: White unctuous mass or almost white flakes or granules; odour, faint and characteristic; taste, bland and mild.

Solubility: Insoluble in *water;* soluble in *alcohol* and in *solvent ether.*

Standards: Stearyl Alcohol is a mixture of solid aliphatic alcohols consisting chiefly of stearyl alcohol.

Melting range: Between 55° and 60°, determined by Method II, Appendix 5.11.

Acid value: Not more than 2.0, Appendix 3.3.15.

Hydroxyl value: Between 195 and 220, Appendix 3.3.17.

Iodine value: Not more than 2.0, Appendix 3.3.18.

Saponification value: Not more than 2.0, Appendix 3.3.20.

Storage: Store in well-closed containers.

Sulphacetamide Eye Drops

Sulphacetamide Sodium Ophthalmic Solution

Category: Antibacterial (ophthalmic).

Usual strengths: 10, 20, 30 per cent w/v.

Standards: Sulphacetamide Eye Drops are a sterile solution of Sulphacetamide Sodium in Purified Water. They contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Sulphacetamide Sodium, $C_8H_9N_2NaO_3S,H_2O$. They may contain suitable buffers, stabilisers and antimicrobial agents.

Identification: Dilute a volume equivalent to about 1 g of Sulpacetamide Sodium to 25 ml with *water,* adjust the pH to between 4 and 5 with *6N acetic acid* and filter. Wash the precipitate with *water* and dry at 105° for two hours; the residue complies with tests (B) and (C) given under Sulphacetamide Sodium.

pH: Between 6.6 and 8.6, Appendix 5.10,

Related substances: Carry out the method for *thin-layer chromatography,* Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 50 volumes of *n-butyl alcohol,* 25 volumes of *ethyl alcohol,* 25 volumes of *water* and 10 volumes of *strong ammonia solution* as the mobile phase. Apply separately to the plate 10 μl of each of the following solutions. For solution (1) dilute the eye drops with *water* to contain 4.0 per cent w/v of Sulphacetamide Sodium. Solution (2) contains 0.20 per cent w/v of *sulphanilamide* in *water.* After removal of the plate, heat it at 105° for 10 minutes, allow to cool and spray with a 2 per cent w/v solution, prepared without heating, of *dimethylaminobenzaldehyde* in a 55 per cent v/v solution of *hydrochloric acid.* Any secondary spot in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (2).

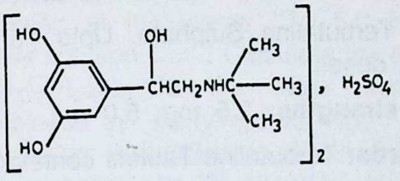
Sterility: Comply with the *test for sterility,* Appendix 4.6.

Assay: To a volume equivalent to 0.5 g of Sulphacetamide Sodium add 75 ml of *water* and 10 ml of *hydrochloric acid* and 3 g of *potassium bromide.* Cool the solution in ice and carry out the method for *nitrite titration,* Appendix 3.3.4. Each ml of *0.1M sodium nitrite* is equivalent to 0.02542 g of $C_8H_9N_2NaO_3S,H_2O$.

Storage: Store in tightly-closed, light-resistant containers in a cool place. The Eye Drops should not be allowed to freeze.

Labelling: The label on the container states (1) the name and concentration of antimicrobial agent used (if any); (2) "NOT FOR INJECTION"; (3) "Use the solution within one month of opening the container; and (4) that the solution should not be used if it is dark brown in colour.

Terbutaline Sulphate



$(C_{12}H_{19}NO_3)_2,H_2SO_4$ Mol. Wt. 548.65

Category: Adrenergic (bronchodilator).

Dose: Upto 15 mg daily, in divided doses.

Description: White or almost white, crystalline powder; odourless or almost odourless.

Solubility: Freely soluble in *water*, slightly soluble in alcohol, practically insoluble in *chloroform* and in *solvent ether.*

Standards: Terbutaline Sulphate is 2-(*tert*-butylamino)-1-(3,5-dihydroxyphenyl)ethanol sulphate. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $(C_{12}H_{19}NO_3)_2,H_2SO_4$, calculated with reference to the dried substance.

Identification: (A) The *infra-red absorption spectrum* of a dispersion in *potassium bromide* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *terbutaline sulphate R.S.* Appendix 5.15B. If not, dissolve the substance in the minimum volume of *methyl alcohol*, evaporate to dryness on a water-bath and obtain a new spectrum of the residue.

(B) The light absorption in the range 230 to 350 nm, of a 1-cm layer of a 0.02 per cent w/v solution in *0.1N hydrochloric acid* exhibits two maxima at about 276 nm and 280 nm, which may be fused. The *extinction* at both 276 nm and 280 nm is about 1.4, Appendix 5.15A.

(C) A solution (1 in 20) gives the reactions of *sulphates*, Appendix 3.1.

Acidity: Dissolve 0.2 g in 10 ml of *carbon dioxide-free water* and titrate with *0.01N sodium hydroxide* using *methyl red solution* as indicator. Not more than 1.2 ml of *0.01N sodium hydroxide* is required to change the colour of the solution to yellow.

Clarity and colour of solution: A 2.0 per cent w/v solution in *water* is clear and the *extinction* of a 4-cm layer of this solution at about 400 nm is not more than 0.22, Appendix 5.15A.

Heavy metals: Not more than 25 parts per million, determined by Method A, Appendix 3.2.4, on a solution obtained in the following manner. Mix 1.6 g with 0.6 g of *anhydrous sodium sulphate* and ignite without melting the sodium sulphate. Cool, add 3.0 ml of *2N hydrochloric acid*, boil and dilute to 50.0 ml with *water.* Cool and filter. Use 25 ml of the filtrate.

ω-*tert*-Butylamino-3,5-dihydroxyacetophenone: The *extinction* of a 2.0 per cent w/v solution in *0.01N hydrochloric acid* at about 330 nm is not more than 0.50, Appendix 5.15A.

Sulphated ash: Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying: Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105° for 3 hours, Appendix 5.8.

Assay: Weigh accurately about 0.4 g and dissolve in a mixture of 60 ml of *glacial acetic acid* and 60 ml of *acetonitrile* with the aid of heat. Cool to room temperature and titrate with *0.05N perchloric acid* using *crystal violet solution* as indicator. Perform a blank determination and make necessary correction. Each ml of *0.05N perchloric acid* is equivalent to 0.02743 g of $(C_{12}H_{19}NO_3)_2,H_2SO_4$.

Storage: Store in tightly-closed, light-resistant containers.

Terbutaline Injection

Terbutaline Sulphate Injection

Category: Adrenergic (bronchodilator).

Dose: Terbutaline Sulphate. By subcutaneous injection, 0.25 to 0.5 mg, four times a day.

Usual Strength: 0.5 mg per ml.

Standards: Terbutaline Injection is a sterile solution of Terbutaline Sulphate in Water for Injection. The solution is filled in containers in which the air is replaced by nitrogen or other inert gas. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $(C_{12}H_{19}NO_3)_2,H_2SO_4$.

Identification: Carry out the method for *thin-layer chromatography,* Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 13 volumes of *isopropyl alcohol,* 5 volumes of *cyclohexane* and 1 volume of *formic acid* as the mobile phase. Apply separately to the plate 2 µl of each of the following solutions. Solution (1) is the injection and solution (2) is a 0.1 per cent w/v solution of *terbutaline sulphate R.S.* in *saline solution.* After removal of the plate allow it to dry in air and spray it with a 2.0 per cent w/v solution of *aminopyrazolone* in *methyl alcohol.* Allow the plate to dry in air and spray with an 8.0 per cent w/v solution of *potassium ferricyanide* in a mixture of 4 volumes of *strong ammonia solution* and 1 volume of *water.* The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

pH: Between 3.0 and 5.0, Appendix 5.10.

Other requirements: Complies with the requirements stated under Injections.

Assay: Measure accurately a volume equivalent to 5 mg of Tebutaline Sulphate and add sufficient *water* to produce 50.0 ml. To 5.0 ml add 35 ml of a buffer solution prepared by dissolving 36.3 g of *tris(hydroxymethyl)aminomethane* in 900 ml of *water,* adjusting the pH to between 9.4 and 9.6 and adding sufficient *water* to produce 1000 ml; add 1.0 ml of a freshly prepared 2.0 per cent w/v solution of *aminopyrazolone* and mix. Add 1.0 ml of a freshly prepared 8.0 per cent w/v solution of *potassium ferricyanide* with vigorous swirling and sufficient buffer solution to produce 50.0 ml. Exactly 75 seconds after the addition of the potassium ferricyanide solution measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 550 nm, Appendix 5.15A, using *water* as the blank. Calculate the content of $(C_{12}H_{19}NO_3)_2,H_2SO_4$ from the *extinction* obtained by repeating the operation using a 0.01 per cent w/v solution of *terbutaline sulphate R.S.* and commencing with the words "To 5.0 ml add 35 ml.........", and from the declared content of $(C_{12}H_{19}NO_3)_2,H_2SO_4$ in the *terbutaline sulphate R.S.*

Storage: Store in single-dose, light-resistant containers in a cool place.

Labelling: The label on the container states that the injection should not be used if the solution is discoloured.

Terbutaline Tablets

Terbutaline Sulphate Tablets

Category: Adrenergic (bronchodilator).

Dose: Terbutaline Sulphate. Upto 15 mg daily, in divided doses.

Usual strengths: 2.5 mg; 5.0 mg.

Standards: Terbutaline Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Terbutaline Sulphate, $(C_{12}H_{19}NO_3)_2,H_2SO_4$.

Identification: (A) Shake a quantity of the powdered tablets equivalent to 20 mg of Terbutaline Sulphate with 50 ml of *0.1N sodium hydroxide* for 10 minutes, dilute to 100 ml with *0.1N sodium hydroxide* and filter. Dilute 20 ml of the filtrate to 50 ml with *0.1N sodium hydroxide.* The light absorption in the range 230 to 350 nm of a 1-cm layer of the resulting solution exhibits a maximum at about 296 nm, Appendix 5.15A.

(B) Carry out the method for *thin-layer chromatography,* Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 13 volumes of *isopropyl alcohol,* 5 volumes of *cyclohexane* and 1 volume of *formic acid* as the mobile phase. Apply separately to the plate 2µl of the following solutions. For solution (1) powder a few tablets and place a quantity equivalent to 10 mg of Terbutaline Sulphate in a centrifuge tube, add 1 ml of a mixture of equal volumes of *alcohol* and *water* and shake for 10 minutes. Centrifuge and use the clear solution. Solution (2) contains 1.0 per cent w/v of *terbutaline sulphate R.S.* in a mixture of equal volumes of *alcohol* and *water.* After removal of the plate, allow it to dry in air and carry out the **Identification** test as described under Terbutaline Injection beginning at the words "and spray with an 8.0 per cent w/v solution......". The principal spot obtained with solution (1) corresponds to the spot in the chromatogram obtained with solution (2).

(C) Shake a quantity of the powdered tablets equivalent to 10 mg of Terbutaline Sulphate with 15 ml of *water* and filter. The filtrate gives the reactions of *sulphates,* Appendix 3.1.

Uniformity of content: Powder one tablet and transfer into a 25-ml volumetric flask, add 15 ml of *0.01N hydrochloric acid* and shake for 10 minutes. Dilute to volume with *0.01N hydrochloric acid* and filter, rejecting the first 5 ml of the filtrate. Dilute, if necessary, a suitable volume of the filtrate with *0.01N hydrochloric acid* to produce a solution containing 0.01 per cent w/v of Terbutaline Sulphate. Carry out the **Assay** described under Terbutaline Injection beginning at the words "To 5.0 ml add 35 ml of a buffer solution.......". Calculate the content of $(C_{12}H_{19}NO_3)_2,H_2SO_4$ in the tablet from the *extinction* obtained by carrying out the **Assay** simultaneously using *terbutaline sulphate R.S.* and from the declared content of $(C_{12}H_{19}NO_3)_2,H_2SO_4$ in the *terbutaline sulphate R.S.*

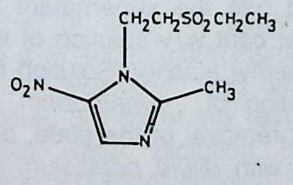
Repeat the operation using a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 85.0 and 115.0 per cent of the average except that for one tablet the content may be between 80.0 and 120.0 per cent of the average.

Other requirements: Comply with the requirements stated under Tablets.

Assay: Weigh and powder 20 tablets. Transfer an accurately weighed portion of the powder, equivalent to about 5.0 mg of Terbutaline Sulphate, into a 50-ml volumetric flask, add 30 ml of *0.01N hydrochloric acid* and shake for 10 minutes. Dilute to volume with *0.01N hydrochloric acid* and shake for filter, rejecting the first 5 ml of the filtrate. Carry out the **Assay** described under Terbutaline Injection beginning at the words "To 5.0 ml add 35 ml of a buffer solution ....".

Storage: Store in tightly-closed, light-resistant containers in a cool place.

Tinidazole



$C_8H_{13}N_3O_4S$ Mol. Wt. 247.26

Category: Antiprotozoal.

Dose: For trichomoniasis, 2 g as a single dose and again after three to five days' rest, if necessary. For giardiasis, 150 mg twice daily for seven days or as a single dose of 2 g. For intestinal ameobiasis, 600 mg twice daily for five to ten days or 2 g as a single dose daily for two to six days. For extraintestinal amoebiasis, 2 g as a single daily dose for 3 days.

Description: Pale-yellow crystals or crystalline powder with a slight characteristic odour.

Solubility: Sparingly soluble in *water;* slightly soluble in *alcohol,* in *chloroform* and in *solvent ether.*

Standards: Tinidazole is 1-[2-(ethylsulphonyl)ethyl]-2-methyl-5-nitro-imidazole. It contains not less than 98.0 per cent and not more than 100.5 per cent of $C_8H_{13}N_3O_4S$, calculated with reference to the dried substance.

Identification: (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *tinidazole R.S.,* Appendix 5.15B.

(B) The light absorption in the range 240 to 350 nm of a 1-cm layer of a 0.001 per cent w/v solution in *methyl alcohol* exhibits a maximum only at about 310 nm; *extinction* at about 310 nm is about 0.35, Appendix 5.15A.

(C) To about 5 mg add 5 ml of *0.1N hydrochloric acid,* 50 mg of *zinc powder,* 4 ml of *hydrochloric acid* and set aside for 30 minutes. Add 4 ml of a 1.0 per cent w/v solution of *vanillin,* heat on a boiling water-bath for 20 minutes, allow to cool to room temperature and dilute to 20 ml with *water.* A greenish-yellow colour is produced.

Melting range: Between 125° and 128°, Appendix 5.11.

Related substances: Carry out the method for *thin-layer chromatography,* Appendix 5.4.3,. using *silica gel GF 254* as the coating substance and a mixture of 95 volumes of *ethyl acetate,* 5 volumes of *methyl alcohol* and 5 volumes of *diethylamine* as the mobile phase. Apply separately to the plate 10 μl of each of the two solutions in a mixture of equal volumes of *chloroform* and *methyl alcohol* containing (1) a 2.0 per cent w/v solution of the substance being examined and (2) a 0.02 per cent w/v solution of the substance being examined. After removal of the plate, allow it to dry in air and examine under ultra-violet lamp having a maximum output at about

254 nm. Any spot in the chromatogram obtained with solution (1) other than the principal spot is not more intense than the spot in the chromatogram obtained with solution (2).

Loss on drying: Not more than 2.0 per cent, determined on 1.0 g by drying in an oven at 100° for 4 hours, Appendix 5.8.

Sulphated ash: Not more than 0.2 per cent, Appendix 3.2.7.

Assay: Weigh accurately about 0.5 g of the substance and dissolve in 30 ml of *acetic anhydride,* add a few drops of *nile blue A solution* and titrate with *0.1N perchloric acid* until a green colour is produced. Perform a blank determination and make necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02473 g of $C_8H_{13}N_3O_4S$.

Storage: Store in well-closed, light-resistant containers.

Tinidazole Tablets

Category: Antiprotozoal.

Dose: Tinidazole. For trichomoniasis, 2 g as a single dose and again after three to five days' rest, if necessary. For giardiasis, 150 mg twice daily for seven days or as a single dose of 2 g. For intestinal amoebiasis, 600 mg twice daily for five to ten days or 2 g as a single dose daily for two to six days. For extraintestinal amoebiasis, 2 g as a single daily dose for 3 days.

Usual strengths: 150 mg; 300 mg; 500 mg.

Standards: Tinidazole Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Tinidazole, $C_8H_{13}N_3O_4S$. The tablets may be coated.

Identification: Extract a quantity of the powdered tablets equivalent to 0.1 g of Tinidazole with *methyl alcohol,* filter and evaporate the filtrate to dryness. The residue complies with the **Identification** test (C) and the test for **Melting range** described under Tinidazole.

Other requirements: Comply with the requirements stated under Tablets.

Assay: Weigh and powder 20 tablets. Weigh accurately a quantity of powder equivalent to about 0.15 g of Tinidazole. Add 20 ml of *methyl alcohol,* shake well and add sufficient *methyl alcohol* to produce 100.0 ml and filter. Dilute 1.0 ml to 100.0 ml with *methyl alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 310 nm, Appendix 5.15A. Calculate the content of $C_8H_{13}N_3O_4S$, taking 356 as the value of E(1 per cent, 1-cm) at the maximum at about 310 nm.

Storage: Store in well-closed, light-resistant containers.

Trimethoprim And Sulphamethoxazole Suspension

Co-trimoxazole Oral Suspension

Category: Antibacterial.

Dose : For children up to one year, Trimethoprim 40 mg and Sulphamethoxazole 200 mg daily. For children one to five years of age, Trimethoprim 80 mg and Sulphamethoxazole 400 mg daily. For adults, Trimethoprim 160 mg to 480 mg and Sulphamethoxazole 800 mg to 2.4 g daily.

Usual strength: Trimethoprim 40 mg and Sulphamethoxazole 200 mg in 5 ml.

Standards: Trimethoprim and Sulphamethoxazole Suspension contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amounts of Trimethoprim, $C_{14}H_{18}N_4O_3$ and Sulphamethoxazole, $C_{10}H_{11}N_3O_3S$.

Identification: Carry out the method for *thin-layer chromatography,* Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 20 volumes of *chloroform,* 2 volumes of *methyl alcohol* and 1 volume of *dimethylformamide* as the mobile phase. Apply separately to the plate 5 μl of each of the following solutions. For solution (1) add 20 ml of *methyl alcohol* to 5 ml of the suspension, mix, shake with 10 g of *anhydrous sodium sulphate,* centrifuge and use the supernatant liquid. Solution (2) is a 2.0 per cent w/v solution of *sulphamethoxazole R.S.* in *methyl alcohol.* Solution (3) is a 0.4 per cent w/v solution of *trimethoprim R.S.* in *methyl alcohol.* After removal of the plate, allow it to dry in air and spray with *dilute potassium iodobismuthate solution.* One of the principal spots in the chromatogram obtained with solution (1) corresponds to the spot obtained in the chromatogram obtained with solution (2) and the other corresponds to the spot in the chromatogram obtained with solution (3).

pH: Between 5.0 and 6.0, Appendix 5.10.

Assay: *For Trimethoprim*—Weigh accurately about 4 g, add 30 ml of *0.1N sodium hydroxide*, shake and extract with four quantities, each of 50 ml, of *chloroform*, washing each extract with two quantities, each of 10 ml, of *0.1N sodium hydroxide*. Reserve the combined aqueous solution and washings for the **Assay** for sulphamethoxazole. Extract the combined chloroform extracts with four quantities, each of 50 ml, of *N acetic acid*. Wash the combined extracts with 5 ml of *chloroform* and dilute the aqueous extracts to 250.0 ml with *N acetic acid*. To 10.0 ml of this solution add 10 ml of *N acetic acid* and sufficient *water* to produce 100.0 ml and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 271 nm, Appendix 5.15A. Calculate the content of $C_{14}H_{18}N_4O_3$, taking 204 as the value of E (1 per cent, 1-cm) at the maximum at about 271 nm. Determine the weight per ml of the suspension and calculate the content of $C_{14}H_{18}N_4O_3$, weight in volume.

For Sulphamethoxazole—Dilute the combined aqueous solution, reserved in the **Assay** for trimethoprim, to 250.0 ml with *water*, filter and dilute 5.0 ml of the filtrate to 200.0 ml with *water* (solution A). Carry out the following procedure protected from light. To 2.0 ml of solution A add 0.5 ml of *4N hydrochloric acid* and 1 ml of a 0.1 per cent w/v solution of *sodium nitrite* and allow to stand for 2 minutes. Add 1 ml of a 0.5 per cent w/v solution of *ammonium sulphamate* and allow to stand for 3 minutes. Add 1 ml of a 0.1 per cent w/v solution of *N-(1-naphthyl) ethylene diamine dihydrochloride* and allow to stand for 10 minutes. Dilute the resulting solution to 25.0 ml with *water* and measure the *extinction* of a 1-cm layer of the solution at about 538 nm, Appendix 5.15 A, using as blank a solution prepared in the same manner but using 2 ml of *water* in place of solution A. Dissolve 0.25 g of *sulphamethoxazole R.S.* in 50 ml of *0.1N sodium hydroxide* and dilute to 250.0 ml with *water*. Dilute 5.0 ml of the resulting solution to 200.0 ml with *water* (solution B). Repeat the procedure using 2.0 ml of solution B and beginning at the words "add 0.5 ml of *4N hydrochloric acid* ....". Calculate the content of $C_{10}H_{11}N_3O_3S$ from the values of the *extinctions* obtained. Determine the weight per ml of the suspension and calculate the content of $C_{10}H_{11}N_3O_3S$, weight in volume.

Storage: Store in tightly-closed, light-resistant containers at a temperature between 15° and 30°. The suspension should not be allowed to freeze.

Labelling: The label on the container states (1) that the contents should be shaken before use; (2) the date after which the contents are not intended to be used; and (3) the storage conditions.

Microcrystalline Wax

Petroleum Wax (microcrystalline); Amorphous Wax

Category: Pharmaceutical aid (stiffening and coating agent).

Description: White or cream-coloured waxy solid; odourless.

Solubility: Insoluble in *water*; sparingly soluble in *ethyl alcohol*; soluble in *chloroform*, in *solvent ether*, in volatile oils and in most warm fixed oils.

Standards: Microcrystalline Wax is a mixture of straight-chain, branched-chain and cyclic hydrocarbons, obtained by solvent fractionation of the still bottom fraction of petroleum by suitable dewaxing or deoiling means.

Melting range: Between 54° and 102°, Appendix 5.11.

Colour: Melt about 10 g on a water-bath, and pour 5 ml of the liquid into a clear-glass (150 mm × 16 mm) bacteriological test-tube; the warm, melted liquid is not darker in colour than a solution made by mixing 3.8 ml of *ferric chloride CS* and 1.2 ml of *cobalt chloride CS* in a similar tube, the comparison being made in reflected light against a white background, the tubes being held directly against the background at such an angle that there is no fluorescence.

Alkalinity: Introduce 35 g into a 250-ml separator, add 100 ml of boiling *water*, and shake vigorously for 5 minutes. Draw off the separated water into a beaker, wash further with two quantities, each of 50 ml, of boiling *water* and add the washings to the beaker. To the pooled washings add one drop of *phenolphthalein solution* and boil; the solution does not acquire a pink colour.

Acidity: If the addition of *phenolphthalein solution* in the test for **Alkalinity** does not produce a pink colour, add 0.1 ml of *methyl orange solution*; no red or pink colour is produced.

Organic acids: To 20 g add 100 ml of a 50 per cent v/v solution of *alcohol*, previously neutralised to *phenolphthalein solution* and titrate rapidly with *0.1N sodium hydroxide*, with vigorous agitation, to a sharp pink end-point. Not more than 0.4 ml of *0.1N sodium hydroxide* is required.

Fixed oils, fats and rosin: Digest 10 g with 50 ml of *sodium hydroxide solution* at 100° for 30 minutes. Separate the water layer and acidify with *2N sulphuric acid*; no oily or solid matter separates.

Ash: Not more than 0.1 per cent, determined on 2.0 g, Appendix 3.3.22. It volatilises without emitting an acrid odour.

Storage: Store in tightly-closed containers.

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APPENDIX 2

Amendments to I.P. Third Edition

2. Biological Tests and Assays

2.12 BIOLOGICAL ASSAY OF OXYTOCIN INJECTION

Page A-26

Delete the word 'INJECTION' from the title

2.13 BIOLOGICAL ASSAY OF VASOPRESSIN INJECTION

Page A-26

Delete the word 'INJECTION' from the title

2.35 TEST FOR HISTAMINE-LIKE SUBSTANCES

Page A-42

Test Animal—Line 2
For '2.5 kg'
read '2.0 kg'

APPENDIX 3

3. Chemical Tests and Assays

3.2.1 Limit Test for Arsenic

Page A-57

Boric Acid—Line 1
For '10 g'
read '1 g'

3.3.7 Assay of Nitrous Oxide

Page A-67

Method—Para 3, Line 2
For 'liquid nitrogen'
read 'liquefied oxygen'

3.3.8 Assay of Oxygen

Page A-67

Method—Line 1
For 'Change'
read 'Charge'

Page A-68

Fig. 1 APPARATUS FOR THE ASSAY OF MEDICINAL GASES

Top right of drawing of Gas Burette
For 'condenser macrometer'
read 'condenser manometer'

3.3.22 Analysis of Vegetable Drugs

Page A-74

Acid-Insoluble Ash

Method II—Line 9
For 'acid-soluble ash'
read 'acid-insoluble ash'

APPENDIX 5

5.5 DETERMINATION OF CONGEALING RANGE OR TEMPERATURE

Page A-120

Method—Line 15

Add the following as a new para after '......per minute'

'If necessary, congelation may be induced by rubbing the inner walls of the test tube with the thermometer, or by introducing a small amount of the previously congealed substance under examination. Pronounced supercooling may result in deviation from the normal pattern of temperature changes. If it happens, repeat the test introducing small fragments of the solid substance under examination at 1° intervals when the temperature approaches the expected congealing point'.

Lines 15-20

Consider the following as a separate paragraph:

'Record the reading ...... after remaining constant'.

5.6 DISINTEGRATION TEST

5.6.1 Disintegration Test for Tablets

Page A-122

Methods

Add the following:

NOTE—If the tablets (uncoated or coated or enteric-coated) adhere to the discs and the preparation fails to comply, repeat the test on a further six tablets omitting the discs. The preparation complies with the test if all the tablets have disintegrated.

Amendments to Addendum I

Page A-3

Contents of Appendices

Appendix 2

BIOLOGICAL TESTS AND ASSAYS

Add the following after '2.24 Biological Assay of Rabies Vaccine'
'2.24 Specific Agglutination Test for Identity of Typhoid and Typhoid Paratyphoid A Vaccines .. A-5'

Appendix 3

CHEMICAL TESTS AND ASSAYS

Add the following after '3.2.1 Limit Test for Arsenic'
'3.2.5 Limit Test for Iron .. A-5'

APPENDIX 5

5. Physical Tests and Determinations

Page A-9

For **'Determinators'**
read **'Determinations'**

APPENDIX 7

7. Reagents and Solutions

7.1 BUFFER SOLUTIONS

Citro-phosphate buffer, pH 7.6—Line 2

Page A-10

For 'water'
read *'water'*

7.4 GENERAL REAGENTS

Nitrate Standard Solution (100 ppm NO_3)—Line 1

Page A-10

For *'Nitrate Standard Solution (100 ppm NO_3)'*
read **'Nitrate Standard Solution (100 ppm NO_3)'**

'Nitrate Standard Solution (2 ppm NO_3)—Line 1

Page A-10

For *'Nitrate Standard Solution (2 ppm NO_3)'*
read **'Nitrate Standard Solution (2 ppm NO_3)'**

Trinitrophenol Solution—Line 2

Page A-11

For 'water'
read *'water'*

Additions

APPENDIX 2

2.43 ASSAY OF PROTAMINE SULPHATE

Reagents

(1) Prepared plasma: Prepare as directed in the *Biological Assay of Heparin Sodium*, Appendix 2.3.

(2) Calcium-thromboplastin solution: Dissolve in a 2 per cent w/v solution of *calcium chloride* a quantity of thromboplastin that is sufficient, as determined by preliminary trial, if necessary, to produce clotting in about 35 seconds in a mixture consisting of equal volumes of *prepared* *plasma* and a mixture of 4 volumes of *saline solution* and 1 volume of the prepared *calcium-thromboplastin solution.*

(3) Heparin solution: On the day of the assay, prepare a solution of *heparin sodium R.S.* in *saline solution* to give a final concentration of 115 Units of heparin activity per ml.

(4) Test solution: Weigh accurately about 25 mg of the preparation being examined and dissolve in sufficient *water for injection* to give a concentration of 1 mg per ml, calculated on dried basis.

Method

Into each of ten very clean tubes (150 mm × 16 mm) add 2.5 ml of *prepared plasma*. Place the tubes in a water-bath at 37 ± 0.2^0, and to each of nine of them add 0.5 ml of *test solution*. Into the tenth tube, which acts as the control, add 2.0 ml of *saline solution* and 0.5 ml of *calcium-thromboplastin solution*, noting the time to the nearest second of adding the latter. Mix with a wire loop and note the time of the first appearance of fibrin fibers to the nearest second. The elapsed time is the normal clotting time of the plasma. Into the nine remaining tubes add 0.43, 0.45, 0.47, 0.49, 0.50, 0.51, 0.53, 0.55, and 0.57 ml respectively of *heparin solution*. To each tube add *saline solution* to make 4.5 ml. Taking the tubes in random order, add 0.5 ml of *calcium-thromboplastin solution*, and note the clotting time in each tube in the same manner as for the control tube. Divide the number of units of heparin activity by the number of mg of Protamine Sulphate in the last tube prior to the first one in which the clotting time is not less than two seconds longer than that in the control tube to calculate the number of units of heparin activity neutralised by 1 mg of Protamine Sulphate, calculated on dried basis.

APPENDIX 3

3.2.1 LIMIT TEST FOR ARSENIC

Preparation of the Test Solution

Add the following at appropriate places on pages indicated against each:

Page A-56

Alginic Acid: Mix 1.5 g with 5 ml of *sulphuric acid AsT,* add a few glass beads and digest in a fumehood, preferably on a hot plate at a temperature not exceeding 120^0, until charring begins. (Additional sulphuric acid may be necessary to wet some specimens completely but the total volume added should not exceed 10 ml). Cautiously add, dropwise, *hydrogen peroxide solution (30 per cent)* allowing the reaction to subside and again heating between addition of drops. Add the first few drops very slowly with sufficient mixing in order to prevent a rapid reaction. Discontinue heating if foaming becomes excessive. When the reaction has abated, heat cautiously, rotating the flask occasionally to prevent the specimen from caking on glass exposed to the heating unit. *Maintain oxidizing conditions at all times during the digestion by adding small quantities of the hydrogen peroxide solution whenever the mixture turns brown or darkens.* Continue the digestion until the organic matter is destroyed, gradually raising the temperature of the hot plate until fumes of sulphur trioxide are copiously evolved and the solution becomes colourless or retains only a light straw colour. Cool, add cautiously 10 ml of *water,* mix, and again evaporate till strong fuming, repeating this procedure to remove any trace of hydrogen peroxide. Cool, add cautiously 10 ml of *Water,* wash the sides of the flask with a few ml of *water,* and dilute with *water* to 35 ml.

Page A-57 **Caramel:** Treat 0.6 g as described under Alginic Acid.

Page A-57 **Ethylcellulose:** Treat 1.0 g as described under Alginic Acid.

Page A-58 **Povidone:** Treat 1.5 g as described under Alginic Acid.

Page A-59 **Propyphenazone:** Mix 0.3 g with 10 ml of a solution of *maqnesium nitrate* in *ethyl alcohol* (1 in 50) in a silica or platinum crucible and ignite the ethyl alcohol and heat gradually to incinerate. If the material remains incompletely carbonised, moisten with a small quantity of *nitric acid AsT,* and ignite again to incinerate. After cooling, add 3 ml of *hydrochloric acid AsT,* heat on a water-bath to dissolve the residue.

Page A-59 **Colloidal Silicon Dioxide:** To 2.5 g contained in a round-bottom flask, add 50 ml of *3N hydrochloric acid* and reflux for 30 minutes. Cool, filter with the aid of suction and transfer the filtrate to a 100-ml volumetric flask. Wash the filter and flask with several portions of hot *water* and add the washings to the volumetric flask. Cool, dilute to volume with *water* and mix. Use 15.0 ml of this solution after adding 3 ml of *hydrochloric acid* for the test.

Page A-59 **Sodium Alginate:** Treat 1.5 g as described under Alginic Acid.

Page A-59 **Sorbic Acid:** Mix 0.5 g with 0.3 g of *anhydrous soldium carbonate AsT,* add 1 ml of *bromine solution AsT,* mix thoroughly and evaporate to dryness on a water-bath. Gently ignite the residue in a porcelain dish, cool, add 5 ml of *water* and 2 ml of *brominated hydrochloric acid AsT* and remove the excess bromine with *stannous chloride solution AsT.*

APPENDIX 5

5.4.4 High Performance Liquid Chromatography

High Performance Liquid Chromatography (HPLC), also known as high pressure liquid chromatography, is essentially a form of column chromatography in which the stationary phase consists of small particle packings contained in a column with a small bore, one end of which is attached to a source of pressurised liquid eluent (mobile phase). With this technique high speed resolution with high sensitivity and reproducibility can be obtained and, unlike in gas-liquid chromatography, non-volatile or thermolabile compounds can be analysed directly.

Apparatus

The apparatus consists of a high-pressure solvent pumping system with a sample injection device attached to one end of a column containing the stationary phase, the other end of which in turn is connected to a sensitive detector and recording system.

The pumping system delivers the mobile phase from one or more reservoirs to the column at a constant rate and at a very high pressure. The composition and flow rate of the mobile phase are stated in the individual monographs. If needed, the composition may be varied in order to obtain a satisfactory chromatograph. Solvents should be of high purity (preferably HPLC grade) and should be filtered through a 0.45 μ filter. It is advisable to have as the mobile phase solvents or solvent mixtures de-aerated using a vacuum pump or other suitable means that will not affect the composition of the mixture. This is necessary to prevent any change in polarity and formation of gas bubbles in the apparatus wihch may alter the flow rate or altogether stop the flow. The sample solution may be introduced directly into the column by injection through a septum or through an injection valve or a fixed-volume loop injector. In another system known as the stop-flow technique, the column flow is stopped and the sample solution is injected into the column when the pressure falls to zero; the port is then closed and the flow is resumed. In the latter system reproducibility is better but zone broadening may occur.

The column is made of stainless steel (the inside may be glass-lined) and is capable of withstanding high pressure. The dimensions are stated in the individual monographs as (length × internal diameter). One end of the column is attached to a suitable detection unit and the other end to a high-pressure pump and sample injection device through high-pressure tubings and connectors. The stationary phase is designated in the individual monographs by a letter which is defined in the list of stationary phases given below.

Unless otherwise specified the detector consists of a low pressure mercury ultra-violet photometer fitted with a low-volume flow cell (about 10 μl); the wavelength setting is specified in the individual monograph.

The detector response is amplified and fed to a suitable recording device, usually a strip-chart potentiometric recorder, where the signal or response is plotted against time. The signal may also be fed to an electronic integrator for the measurement of chromatogram peak areas.

Method

Prepare the solutions described in the individual monographs and ensure that they do not contain any solid particles. Proceed as described under gas-liquid chromatography, Appendix 5.4.1.

NOTE — In tests and assays requiring gradient elution, peak area determinations are to be used.

Stationary phases

L1 — Octadecylsilane chemically bonded to porous silica or ceramic micro-particles, 5 to 10 μm in diameter.

L2 — Octylsilane chemically bonded to totally porous silica particles, 5 to 10 μm in diameter.

L3 — Porous silica particles, 5 to 10 μm in diameter.

5.20 DETERMINATION OF WATER BY AZEOTROPIC DISTILLATION

Apparatus

The apparatus (see Fig. 7) consists of a round-bottomed, 500-ml flask (A) connected by means of a trap (B), 23.5 to 24.0 cm long, to a verticle

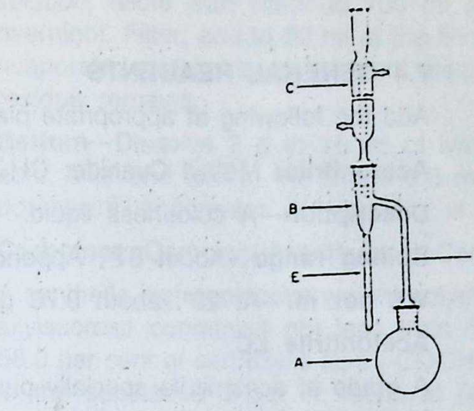

Fig. 7 APPARATUS FOR THE DETERMINATION OF WATER BY AZEOTROPIC DISTILLATION

reflux condenser of the straight-tube type (C), by ground-glass joints. The condenser is approximately 40 cm long and has a bore diameter of not less than 8 mm. The connecting tube (D) is 9 to 11 mm in internal diameter. The receiving tube (E) has a 5-ml capacity and its cylindrical part, 14.6 to 15.6 cm in length, is graduated in 0.1-ml sub-divisions. The flask is heated in an oil-bath or in an electric mantle. The upper portion of the flask and the connecting tube may be insulated.

Before use, the condenser and receiving tube should be cleaned with *chromic acid mixture*, thoroughly rinsed with *water* and dried in an oven. Prepare the toluene to be used by shaking a suitable volume of *toluene* with a small quantity of *water*, separating the excess water and distilling.

Method

Weigh accurately a quantity of the substance being examined, that is expected to yield 2 to 4 ml of *water* and transfer to the dry flask. If the substance is semi-solid, weigh it in a metal foil, fold the foil carefully and pass it through the neck of the flask. To prevent bumping add enough washed and dried sand to cover the bottom of the flask or a few capillary melting-point tubes, 10 cm long, sealed at the upper end. Add about 200 ml of the prepared toluene, connect the apparatus and fill the receiving tube (E) with toluene poured through the top of the condenser. Heat the flask gently for 15 minutes and when the toluene begins to boil, distil at the rate of about 2 drops per second until most of the water has distilled over, then increase the rate to about 4 drops per second. When the water has apparently completely distilled over, rinse the inside of the condenser tube with toluene with the aid of a tube brush attached to a copper wire and saturated with toluene. Continue the distillation for 5 minutes, remove the heat and allow the receiving tube to cool to room temperature. If any droplets of water stick to the walls of the receiving tube, scrub them using a copper wire with a rubber band wrapped round it and washed with toluene. After complete separation of the water and toluene in the tube, read off the volume of water in the tube and calculate the content of water as percentage w/w. assuming the weight per ml of water to be 1.0.

APPENDIX 7

7.4 GENERAL REAGENTS

Add the following at appropriate places on pages indicated against each:

Page A-154 **Acetonitrile:** Methyl Cyanide; CH_3CN = 41.05

Description—A colourless liquid.

Boiling range—About 81°, Appendix 5.3.

Wt. per ml—At 20°, about 0.78 g, Appendix 5.19.

Page A-154 **Acetonitrile LC**

A grade of acetonitrile specially purified for use in liquid chromatography having a minimum transmittance of 80 per cent at about 210 nm and 97 per cent at about 230 nm, using *water* in the reference cell.

Page A-154 **Acetonitrile UV**

Spectrophotometric grade of commerce having a minimum transmittance of 98 per cent in the range 255 to 420 nm, using *water* in the reference cell.

Page A-156 **Alkaline Phosphatase Enzyme**

Analytical reagent grade of commerce.

Page A-156 **Alkaline Phosphatase Solution**

Transfer 3.1 g of *boric acid* to a 1000-ml volumetric flask containing 500 ml of *water*, add 21 ml of *N sodium hydroxide* and 10 ml of 2.0 per cent w/v solution of *magnesium chloride*, dilute to volume with *water*, and mix. Adjust pH of the solution to 9.0 ± 0.2 by addition of *N sodium hydroxide* or *N hydrochloric acid*, as necessary (solution A).

Dissolve 0.1 g of *alkaline phosphatase enzyme* in 40 ml of solution A in a 50-ml volumetric flask, dilute to volume with solution A and mix. *Prepare the solution fresh daily.*

Page A-167 **Calcium Acetate:** $Ca(C_2H_3O_2),H_2O$ = 176.18

Description—White, crystalline granules or powder.

Solubility—Freely soluble in *water*; slightly soluble in *alcohol*.

Insoluble matter—Dissolve 10.0 g in 100 ml of *water*, filter and wash the insoluble matter with *water*. The residue, dried at 105°, weighs not more than 1.0 mg.

Alkalinity—Dissolve 2.0 g in 25 ml of *water* and add 2 drops of *phenolphthalein solution*; no pink colour is produced.

Chloride—1 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Nitrate—Dissolve 1.0 g in 10 ml of *water*, add 5 mg of *sodium chloride*, 0.05 ml of *indigo carmine solution* and, with stirring, 10 ml of *nitrogen-free sulphuric acid*. A blue colour is produced which persists for 10 minutes.

Sulphate—1 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Alkalies and magnesium—Dissolve 1 g in 50 ml of *water*, add 2 ml of *hydrochloric acid*, heat to boiling, and add 35 ml of a 5 per cent solution of *oxalic acid.* Cool, neutralise the solution slowly with *strong ammonia solution*, dilute with *water* to 100 ml and allow to stand for 4 hours or overnight. Filter, and to 50 ml of the filtrate, add 5 drops of *sulphuric acid*, evaporate, and ignite to constant weight. Not more than 1.5 mg of the residue remains.

Barium—Dissolve 2 g in 15 ml of *water*, add 2 drops of *glacial acetic acid*, filter and add to the filtrate 0.3 ml of a 10 per cent w/v solution of *potassium dichromate.* No turbidity is produced within 10 minutes.

Page A-169

Carbomer: Carboxypolymethylene; Carbomer 934P

A synthetic high molecular weight polymer of acrylic acid cross-linked with allylsucrose containing not less than 56.0 per cent and not more than 68.0 per cent of carboxylic acid (-COOH) groups, calculated with reference to the substance dried 'in vacuo at 80°' for 1 hour.

Description—White, fluffy powder; odour, slight and characteristic; hygroscopic.

Solubility—When neutralised with alkali hydroxides or amines, soluble in *water*, in *alcohol*, and in *glycerin.*

Acidity or alkalinity—A 1 per cent w/v dispersion produces an orange colour with *thymol blue solution* and a yellow colour with *cresol red solution* (pH about 3).

Viscosity—Between 29400 and 39400 centipoises, when determined by the following method.

Fix a stirrer capable of running at a speed of 1000 ± 10 rpm in a 1000-ml beaker containing 500 ml of *water* so that the shaft is at an angle of 60° and to one side of the beaker and the propeller is near the bottom of the beaker. While stirring continuously, add 2.5 g carefully and with uniform rate over a period of 45 to 90 seconds, ensuring that loose aggregates of powder are broken up, and continue stirring at 1000 ± 10 rpm for 15 minutes. Remove the stirrer, and place the beaker with its contents in a water-bath maintained at 25° ± 0.2° for 30 minutes. Insert the stirrer to a depth necessary to ensure that air is not drawn into the dispersion and continue stirring at 300 ± 10 rpm. Titrate with a calomel-glass electrode system to a pH of 7.5 ± 0.3 by adding an 18 per cent w/v aqueous solution of *sodium hydroxide* below the surface, the end-point being determined potentiometrically. (Approximately 6.2 ml of the sodium hydroxide solution will be required). Allow 2 to 3 minutes before final determination of pH. If the final pH exceeds 7.8, discard the mucilage and redetermine it by using lesser quantity of the sodium hydroxide solution for titration. Place this mucilage in the water-bath at 25° for 1 hour, and determine its viscosity by Method C, Appendix 5.18, without delay to avoid slight viscosity changes possible after 75 minutes of alkali addition. Equip a suitable rotating viscometer with a spindle having a cylinder of 1.47 cm diameter and 0.16 cm height attached to a shaft of 0.32 cm diameter, the distance from the top of the cylinder to the lower tip of the shaft being 3.02 cm, and the immersion depth being 4.92 cm (No. 6 spindle). Rotate the spindle at 20 rpm and record the scale reading on the viscometer. Calculate the viscosity in centipoises by multiplying the scale reading with spindle constant at 20 rpm.

Page A-170

Ceric Ammonium Nitrate: Ammonium Ceric Nitrate; $Ce(NO_3)_6(NH_4)_2$ = 548.23

General reagent grade of commerce

Page A-172

Chloride Solution, Standard

Dilute 1.0 ml of a 0.0824 per cent w/v solution of *sodium chloride* to 100.0 ml with *water*

Page A-180

Dimethylaminobenzaldehyde Reagent

Dissolve 0.2 g of *dimethylaminobenzaldehyde* in 20 ml of *alcohol* and add 0.5 ml of *hydrochloric acid*. Shake the solution with *decolorising charcoal* and filter. The colour of the filtrate should not be more intense than that of a *0.0002N iodine.*

NOTE—The reagent must be freshly prepared.

Page A-180

2,6-Dimethylaniline: 2,6-Xylidine; $C_8H_{11}N$ = 121.18

Description—Yellow liquid.

Solubility—Sparingly soluble in *water;* soluble in *alcohol* and in mineral acids.

Refractive Index—About 1.5609 at 20°, Appendix 5.14.

Wt. per ml—At 20°, about 0.98, Appendix 5.19.

Page A-181

N,N-Dimethyl-*p*-phenylenediamine Dihydrochloride: $(CH_3)_2NCH_4NH_2,2HCl$ = 209.12

Contains not less than 98.0 per cent of $C_3H_{12}N_2,2HCl$.

Description—White, fine crystalline powder; hygroscopic.

Solubility—Freely soluble in *water;* soluble in *alcohol.*

Assay—Dissolve about 400 mg in about 75 ml of *water* in a 250-ml beaker. Titrate with *0.IN sodium hydroxide,* using *methyl red solution* as indicator. Each ml of *0.IN sodium hydroxide* is equivalent to 0.01046 g of $C_3H_{12}N_2,2HCl$.

Page A-181

Dimethyl Phthalate: $C_{10}H_{10}O_4$ = 194.19

Contains not less than 99.0 per cent and not more than 100.5 per cent w/w of $C_{10}H_{10}O_4$.

Description—Colourless or faintly coloured liquid; odourless or almost odourless.

Solubility—Slightly soluble in *water;* miscible with *alcohol,* with *solvent ether* and with most organic solvents.

Acidity—Mix 20 ml with 50 ml of *alcohol* previously neutralised to *phenolphthalein solution.* Not more than 0.1 ml of *0.IN sodium hydroxide* is required to neutralise the solution, using *phenolphthalein solution* as indicator.

Wt. per ml—At 20°, about 1.19, Appendix 5.19.

Assay—Carry out the method for the *determination of esters,* Appendix 3.3.2, using 1.5 g and 50 ml of *0.5N alcoholic potassium hydroxide.* Each ml of *0.5N alcoholic potassium hydroxide* is equivalent to 0.04855 g of $C_{10}H_{10}O_4$.

Page A-185

Ethylene Glycol: Ethane-1,2-diol; $HOCH_2CH_2OH = 62.07$

Description—Clear, colourless, slightly viscous liquid; practically ordourless; hygroscopic.

Solubility—Miscible with *water* and with *alcohol;* slightly soluble in *solvent ether;* practically insoluble in *benzene.*

Wt. per ml—At 20°, about 1.11 g, Appendix 5.19.

Boiling range—Between 194° and 200°, Appendix 5.3.

Residue on ignition—Not more than 0.005 per cent w/w when ignited to constant weight.

Acidity—Add 0.2 ml of *phenol red solution* to 50 ml of *water,* and titrate with *0.1N sodium hydroxide* to a red end-point. Add 50 ml (55 g) of the sample and titrate with *0.1N sodium hydroxide.* Not more than 1 ml is required to restore the red colour.

Chloride—4.5 ml (5 g) complies with the *limit test for chlorides,* Appendix 3.2.2.

Water—Not more than 0.2 per cent, Appendix 3.3.25.

Page A-187

Gastric Juice, Simulated

Dissolve 2.0 g of *sodium chloride* and 3.2 g of *pepsin* in 7.0 ml of *hydrochloric acid.* Dilute with sufficient *water* to produce 1000 ml. The pH of the solution should be about 1.2.

NOTE—Pepsin may be omitted where indicated in any test.

Page A-198

Magnesium Chloride

Of the Indian Pharmacopoeia.

Page A-200

Metalphthalein: Phthalein purple; $C_{32}H_{32}N_2O_{12}$ + aq.

Description—Creamy-white to brown powder.

Sensitivity—Dissolve 10 mg in 1 ml of *strong ammonia solution* and dilute to 100 ml with *water.* To 5 ml of the solution add 95 ml of *water,* 4 ml of *strong ammonia solution,* 50 ml of *alcohol* and 0.2 ml of *0.1N barium chloride;* the solution is bluish-violet. Add 0.24 ml of *0.05M disodium edetate;* the solution becomes colourless.

Page A-203

1,3-Naphthalenediol: 1,3-Dihydroxynaphthalene; Naphthoresorcinol; $C_{10}H_8O_2 = 160.17$

Description—Greyish-white to tan crystals or powder.

Solubility—Freely soluble in *methyl alcohol;* sparingly soluble in *alcohol,* in *water,* and in *solvent ether.*

Melting range—Between 122° and 127°, Appendix 5.11.

Page A-203

2-Naphthol-6,8-disodium Disulphonate: Naphthol Sodium Disulphonate; G salt; $C_{10}H_6Na_2O_7S_2 = 348.25$

Description—White or slightly brown crystalline powder.

Solubility—Freely soluble in *water;* insoluble in *alcohol.*

Loss on drying—Not more than 5.0 per cent, when dried to constant weight at 105°, Appendix 5.8.

Residue on ignition—Weigh accurately about 0.7 g, previously dried at 105^0 for 3 hours. Add 2 ml of *sulphuric acid*, and carefully ignite until the residue is white or nearly so. Cool, add 0.5 ml of *sulphuric acid* and 1 ml of *nitric acid*, evaporate, and ignite to constant weight. The weight of sodium sulphate so obtained corresponds to between 40.0 per cent and 44.0 per cent of the weight of the dried substance taken.

Page A-204

Ninhydrin Reagent

Dissolve 272 g of *sodium acetate* in 250 ml of *water* by heating to 35^0, cool and add slowly 50 ml of *glacial acetic acid* and sufficient *water* to produce 500 ml (stock solution A). Dissolve 4 g of *ninhydrin* in 100 ml of *2-methoxyethanol*, shake gently with 1 g of cation exchange resin (hydrogen form) (Dowex 50 is suitable) and filter. Add this solution to 100 ml of a 0.16 per cent w/v solution of *stannous chloride* in stock solution A.

NOTE—Ninhydrin Reagent must be freshly prepared.

Page A-204

Ninhydrin-Stannous Chloride Reagent

To 0.2 g of *ninhydrin* dissolved in 4 ml of hot *water* add 5 ml of a 0.16 per cent w/v solution of *stannous chloride*. Allow the mixture to stand for 30 minutes, filter and store at 2° to 8°. Dilute 2.5 ml of the solution with 5 ml of *water* and 4 ml of *isopropyl alcohol* immediately before use.

Page A-207

Palladium Chloride Reagent

Dissolve with gentle heating 0.2 g of *palladium chloride* in 116 ml of *N hydrochloric acid*. Cool, add 13.6 g of *sodium acetate* and dilute to 1000 ml with *water*.

Page A-218

Potassium Iodide-Starch Solution, Alcoholic

Dissolve 1 g of *potassium iodide* in sufficient *water* to produce 100 ml. Triturate separately 3 g of *soluble starch* in 10 ml of cold *water* and add the mixture to 90 ml of boiling *water* with constant stirring. Just before use, mix 10 ml of each of the solutions with 3 ml of *alcohol*.

Page A-226

Sodium Butanesulphonate: Butanesulphonic acid sodium salt; $C_4H_9NaO_3S$ = 160.20

General reagent grade of commerce.

Page A-227

Sodium Formate: HCO_2Na = 68.01

Description—White, crystalline powder.

Solubility—Soluble in *water*, slightly soluble in *alcohol*.

Chloride—2 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate—Dissolve 1 g in 10 ml of a 25 per cent v/v solution of *hydrochloric acid* in *water* and evaporate to dryness. Dissolve the residue in a further 10 ml of the dilute hydrochloric acid, again evaporate to dryness, and repeat the solution and evaporation once more; the residue complies with the *limit test for sulphates*, Appendix 3.2.8.

Loss on drying—Not more than 1.0 per cent, when dried to constant weight at 130^0, Appendix 5.8.

Page A-238

o-**Tolidine:** 3,3′-Dimethyl-(1,1′-diphenyl)-4,4′-diamine; $(NH_2)(CH_3)C_6H_3.C_6H_3(CH_3)(NH_2)$; $C_{14}H_{16}N_2 = 212.29$

Description—White to reddish crystals or crystalline powder.

Solubility—Slightly soluble in *water*, soluble in *alcohol,* in *solvent ether*, and in dilute acids.

Melting range—Between 129^0 and 131^0, Appendix 5.11.

Storage—Store in well-closed containers, protected from light.

Page A-239

Tris(hydroxymethyl)aminomethane: 2-Amino-2-(hydroxymethyl)-1,3-propanediol; Tromethamine; THAM; $C_4H_{11}NO_3 = 121.14$

Description—White crystals or crystalline powder; odour, characteristic.

Solubility—Freely soluble in *water* and in low molecular weight aliphatic alcohols; practically insoluble in *chloroform,* in *benzene,* and in *carbon tetrachloride.*

Melting range—Between 168^0 and 172^0, Appendix 5.11.
pH—Between 10.0 and 11.5, determined in a 10 per cent w/v solution, Appendix 5.10.

Loss on drying—Not more than 1.0 per cent, when dried to constant weight at 105^0, Appendix 5.8.

Residue on ignition—Not more than 0.1 per cent w/w, when ignited to constant weight.

Assay—Weigh accurately about 0.25 g and dissolve in 100 ml of *water.* Add a few drops of *bromocresol purple solution* and titrate with *0.1.N hydrochloric acid* to a yellow end-point. Each ml of *0.1N hydrochloric acid* is equivalent to 0.01211 g of $C_4H_{11}NO_3$.

7.5 VOLUMETRIC REAGENTS AND SOLUTIONS

Page A-244

Barium Chloride, 0.1N: $BaCl_2,2H_2O = 244.27$

Dissolve 12.2 g of *barium chloride* in sufficient *carbon dioxide-free water,* to produce 1000 ml and standardise the solution as follows:

To 10 ml of the solution add 60 ml of *water*, 3 ml of *strong ammonia solution* and 0.5 to 1 mg of *metalphthalein* as indicator and titrate with *0.05M disodium edetate.* As the solution begins to decolorise, add 50 ml of *alcohol* and titrate until the solution is decolorised. Each ml of *0.05M disodium edetate* is equivalent to 0.012215 g of $BaCl_2,2H_20$.

Page A-244

Ceric Ammonium Nitrate, 0.1N: Ammonium Ceric Nitrate, 0.1N; $Ce(NO_3)_6(NH_4)_2 = 548.23$; 54.82 g in 1000 ml.

Shake a solution containing 56 ml of *sulphuric acid* and 55 g of *ceric ammonium nitrate* for 2 minutes and carefully add five successive 100-ml quantities of *water* shaking after each addition. Adjust the volume to 1000 ml by addition of *water.* Standardize the solution as follows:

To 25 ml of the solution add 5 ml of *sulphuric acid* and 0.15 ml *osmic acid solution* and titrate with *0.025N sodium arsenite,* using *ferroin sulphate solution* as indicator. Each ml of *0.025N sodium arsenite* is equivalent to 0.05482 g of $Ce(NO_3)_6(NH_4)_2$.

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(Combined for Addendum I and Addendum II)

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